No. 78-605

In the Supreme Court of the United States

OCTOBER TERM, 1978

UNITED STATES OF AMERICA, ET AL., PETITIONERS

v.

GLEN L. RUTHERFORD, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT

BRIEF FOR THE UNITED STATES

WADE H. MCCREE, JR.
Solicitor General

JOHN H. SHENEFIELD
Assistant Attorney General

STEPHEN R. BARNETT
Deputy Solicitor General

ELINOR HADLEY STILLMAN
Assistant to the Solicitor General

BARRY GROSSMAN
PETER L. DE LA CRUZ
Attorneys
Department of Justice
Washington, D.C. 20530

RICHARD M. COOPER
Chief Counsel

EUGENE M. PFEIFER
Associate Chief Counsel for Enforcement
Food and Drug Administration
Department of Health, Education and Welfare
Rockville, Maryland 20852

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-7a) is reported at 582 F.2d 1234. The opinion of the district court (Pet. App. 11a-44a) is reported at 438 F. Supp. 1287. The decision of the Commissioner of Food and Drugs (Pet. App. 45a-274a) is reported at 42 Fed. Reg. 39768.

JURISDICTION

The judgment of the court of appeals (Pet. App. 8a-9a) was entered on July 10, 1978. On August 4,

1978, the court of appeals summarily denied a Motion for Clarification or in the alternative Petition for Re-Hearing filed by respondents (Pet. App. 10a). The petition for a writ of certiorari was filed on October 10, 1978, and granted on January 22, 1979. The jurisdiction of this Court rests on 28 U.S.C. 1254(1).

QUESTIONS PRESENTED

1. Whether the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act apply to drugs intended for use by the terminally ill.

2. Whether the judgment of the court of appeals barring application of the Federal Food, Drug, and Cosmetic Act to interstate distribution of the drug Laetrile for intravenous administration to terminally ill cancer patients is sustainable on the ground that Laetrile is exempt from the premarketing clearance requirements of the Act by operation of the Act's 1962 grandfather clause.

3. Whether the judgment of the court of appeals is sustainable on the ground that prohibition of the interstate distribution of Laetrile violates a constitutional right of privacy.[1]

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[1] Questions 2 and 3 are issues reached by the district court but not by the court of appeals. As we noted in our petition for certiorari (Pet. 18), respondents can be expected to argue that the judgment of the court of appeals should be affirmed on the grounds relied on by the district court. See *United States* v. *New York Telephone Co.*, 434 U.S. 159, 166 n.8 (1977). For that reason we address those issues here. In view of the importance of this case to the federal system of drug regulation and the need to secure a final resolution of the issues after four years of litigation, we urge the Court to decide all of the issues here in the event it concludes that the court of appeals' reasoning is erroneous.

STATUTES INVOLVED

The pertinent portions of Sections 201(p) and 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(p) and 355, and Section 107(c)(4) of the Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789 ("1962 grandfather clause"), are reproduced at Pet. 2-5.

STATEMENT

A. Initial Court Proceedings

Section 505 of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 355, prohibits the interstate distribution of any "new drug," as defined in Section 201(p) of the Act, 21 U.S.C. 321(p), unless (1) a new drug application (NDA), supported by appropriate evidence of the drug's safety and effectiveness, has been approved by the Secretary of Health, Education and Welfare, or (2) the drug is exempted from the approval requirements by one of the Act's two "grandfather" provisions.[2] The Secre-

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[2] Under the 1938 Act, a "new drug" was one not generally recognized by qualified experts as safe for its intended use (Section 201(p), 52 Stat. 1041). The Act contained a "grandfather clause" excluding from the definition of "new drug" any drug which, before enactment of the 1938 Act, was subject to the Pure Food and Drugs Act of 1906 (ch. 3915, 34 Stat. 768), and for which representations concerning the conditions of use were identical to those made for its use before the 1938 Act was enacted. This 1938 grandfather clause remains in the current Act. 21 U.S.C. 321(p)(1).

The 1962 Amendments also contain a grandfather clause, excluding from the definition of "new drug" any drug that, on October 9, 1962 (the day immediately preceding the enact-

tary has delegated his approval authority to the Commissioner of Food and Drugs (the Commissioner), who directs the Food and Drug Administration (FDA). 21 C.F.R. 5.1(a)(1).

This case concerns a group of drugs that differ in chemical composition but are known, or have been known, by the name Laetrile (Pet. App. 58a-69a).[3] Alleging that the proponents of Laetrile in its various forms had not established either that it was entitled to grandfather status or that it met the statutory requirements for approval as a new drug, the FDA brought a series of civil and criminal actions to prevent the introduction of Laetrile, under various names and in various forms, into interstate commerce.[4]

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ment of the 1962 Amendments): "(A) was commercially used or sold in the United States, (B) was not a new drug [under the 1938 Act] * * *, and (C) was not covered by an effective [new drug] application." Section 107(c)(4), 76 Stat. 789.

[3] Some of these drugs have also been known by other names —for example, "amygdalin" (see discussion at pages 6-7, *infra*). For the sake of convenience we will use only the name Laetrile, unless discussion of a particular point requires distinguishing among different names or formulations.

[4] *E.g., United States* v. *Turner*, 558 F.2d 46 (2d Cir. 1977) (criminal prosecution for conspiracy to import Laetrile); *United States* v. *Westover*, 511 F.2d 1154 (9th Cir.), cert. denied, 422 U.S. 1009 (1975) (criminal prosecution for conspiracy to import); *United States* v. *Articles of Food and Drug*, 449 F. Supp. 497 (E.D. Wisc. 1978) and 441 F. Supp. 772 (E.D. Wisc. 1977) (civil seizure action); *United States* v. *Spectro Foods Corp.*, Civ. No. 76-101 (D. N.J. Jan. 29, 1976), aff'd in pertinent part, 544 F.2d 1175 (3d Cir. 1976) (civil injunctive suit); *United States* v. *General Research Laboratories*, 397 F. Supp. 197 (C.D. Cal. 1975) (civil injunctive suit). Earlier unreported decisions are published in the Drug and Device Notices of Judgment (D.D.N.J.) published by the FDA under the authority of 21 U.S.C. 375(a). See, *e.g., United States* v. *An Article of Drug . . . Laetrile (Krebs Laboratories) etc.* (D. Ida. Apr. 30, 1965), D.D.N.J. No. 8507 (Sept. 1966) (civil condemnation suit); *United States* v. *Hawk et al.* (S.D. Cal. Feb. 23, 1963), D.D.N.J. No. 8082 (July 1965) (civil injunctive suit).

In March 1975, respondents instituted the present suit to enjoin the government from interfering with the sale and distribution of Laetrile by the filing of additional injunctive, seizure, or criminal actions (A. 7-11).[5] In August 1975 the district court issued a preliminary injunction that enjoined the government from preventing the purchase and subsequent interstate movement of a limited quantity of Laetrile for Glen L. Rutherford, one of the plaintiffs (A. 18-19).[6] The court of appeals did not disturb this injunction, but instructed the district court to remand the case to the Commissioner for the development of an adminis-

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[5] The suit was originally instituted by Juanita Stowe, a cancer patient, and her husband Jimmie Stowe. After Mrs. Stowe's death, an amended complaint was filed by two other patients, Glen L. Rutherford and Phyllis S. Schneider, and Mrs. Schneider's husband, on behalf of a class composed of cancer patients and their spouses who are responsible for the costs of treatment. Mrs. Schneider subsequently died. By order entered April 8, 1977, the district court certified this case as a class action on behalf of a class composed of terminally ill cancer patients (A. 47-58). That order was not appealed by the government.

[6] The district court subsequently entered similar orders on behalf of others who showed, by affidavit, that they were members of the certified plaintiff class of terminally ill cancer patients (A. 1-6).

trative record addressing the issues whether Laetrile is a new drug within the meaning of Section 201(p) of the Act and, if so, whether it is exempt from the premarketing approval requirements by virtue of either the 1938 or the 1962 grandfather clause (A. 31-41).

B. Administrative Proceedings on Remand

The Commissioner initiated administrative proceedings through a Federal Register announcement seeking public comment, and provided individual notice to certain interested persons known to be Laetrile proponents (Pet. App. 47a-49a; 42 Fed. Reg. 10066-10069 (1977)). The proceedings included two days of public hearings and produced more than four hundred submissions, totaling more than five thousand pages, from diverse sources. On July 29, 1977, the Commissioner issued his opinion (Pet. App. 45a-274a).

1. The Commissioner found that the controversy concerns a number of different drugs (*i.e.*, drugs consisting of different chemical compounds) that are referred to by a number of different names, including "Laetrile," "laetrile(s)," "amygdalin," and "vitamin B-17" (Pet. App. 58a-73a). The drugs either consist at least in part of a specific chemical compound known as "amygdalin" (a glucoside present in the kernels or seeds of most fruits) or are related in some way to that compound (Pet. App. 58a-59a, 62a-66a). The proper chemical name for amygdalin is D-mandelonitrile-*beta*-D-glucosido-6-*beta*-D-glucoside (Pet. App. 63a). Amygdalin thus differs in chemical structure from a compound that Ernst T. Krebs, Jr., prepared in 1952 and named "Laetrile" (Pet. App. 63a-64a). That compound was identified by Krebs, one of the proponents of Laetrile, as a substance for which the chemical name is l-mandelonitrile-*beta*-glucuronoside (Pet. App. 65a). Despite the difference in chemical structure, proponents and opponents of the drugs in controversy have used the terms "laetrile" and "Laetrile" interchangeably with the term "amygdalin" for the compounds described above and even for somewhat different compounds (Pet. App. 66a, 69a). The Commissioner concluded that there is no uniform definition of the proper noun "Laetrile" (Pet. App. 69a) and that the term "laetrile" is in practice a "broad or generic term for a group of compounds of unknown number" (Pet. App. 70a). Chemical identification of a particular drug is essential to proving claims that it is not a new drug, that it comes within one of the grandfather clauses of the Act, or that it meets safety and effectiveness requirements for new drugs (Pet. App. 104a, 166a, 180a-181a).

2. The Commissioner concluded that Laetrile in its various forms is a "drug" as defined in the Act, because it is being sold for the cure or prevention of disease within the meaning of Section 201(g)(1) of the Act, 21 U.S.C. 321(g)(1) (Pet. App. 245a-247a). In determining whether Laetrile is a "new drug"—*i.e.*, one not generally recognized by qualified experts as safe and effective for its suggested use (Section

201(p) of the Act, 21 U.S.C. 321(p))—the Commissioner applied the statutory criteria recognized by this Court in *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629-632, 652 (1973). The Commissioner reviewed the record both for controlled investigations, conducted by qualified experts and published in the scientific literature, establishing the safety and effectiveness of the drug, and for the views of experts, based on that evidence, that the drug is safe and effective (Pet. App. 89a-93a).

A review of the scientific literature throughout the world failed to produce reliable information from which experts could make a determination concerning Laetrile's safety (Pet. App. 155a-157a). Experts testified that there were no adequate scientific studies of the safety or toxicity of Laetrile in any method of administration, either when taken alone or in conjunction with other cancer drugs (Pet. App. 155a-157a, 271a). They testified that there were, nonetheless, definite indications that oral administration of Laetrile is toxic (*id.* at 157a-162a; see *id.* at 254a-257a), a danger that Laetrile's proponents had themselves recognized in their earlier labeling of the drug (*id.* at 86a-88a, 158a, 254a-255a).[7]

[7] Documents relating to FDA reviews of applications submitted in 1962 and 1970 for approval of the use or marketing of Laetrile were included in the record. On October 3, 1962, Ernst T. Krebs, Jr., submitted NDA's for two Laetrile formulations to be administered in a series of injections for the treatment of cancer (Pet. App. 191a-192a, 197a, 203a-204a). Neither was approved, because of the lack of data showing safety and effectiveness. *Id.* at 203a-204a; see page 28, note 14, *infra*. In 1970, the McNaughton Foundation submitted a notice of claimed investigational exemption for Laetrile under which it would be allowed to conduct studies in humans. The FDA denied permission to conduct tests because the data supplied to show safety were inadequate to justify use of the drug in humans. *Id.* at 155a-156a.

The Commissioner accordingly found that Laetrile had not been adequately tested for safety and that it was not generally recognized among experts as safe for use in man (Pet. App. 154a-162a).[8]

The Commissioner reached similar conclusions with respect to the drug's effectiveness. Data submitted for the record by Laetrile proponents failed to meet the standards prescribed for controlled clinical investigations of drug effectiveness. With respect to studies on humans, the Commissioner found that "[t]here are

[8] Reports appearing in the medical literature after the administrative hearing support the toxicity findings regarding oral Laetrile and raise new questions about the toxicity of the injectable form of the drug. See Humbert, et al., *Fatal Cyanide Poisoning: Accidental Ingestion of Amygdalin*, 238 JAMA 482 (1977). The authors report the death of an 11-month-old girl who accidentally ingested from one to five 500 mg. amygdalin tablets. See also Lewis, *Laetrile*, 127 West J. Med. 55 (1977), for a report on 25 cases of cyanide toxicity associated with the use of articles containing amygdalin; and Schmidt, et al., *Laetrile Toxicity Study in Dogs*, 239 JAMA 943 (1978).

For findings not limited to the oral form, see Smith, et al., *Laetrile Toxicity: A Report of Two Cases*, 238 JAMA 1361 (1977). The authors report that toxicity was associated with use of both the oral and injectable forms of Laetrile. Symptoms disappeared after Laetrile was discontinued. In one case the patient reinstituted self-medication with Laetrile against medical advice, and symptoms of rash, fever, malaise, headache and severe abdominal cramps reappeared. Laetrile was again withdrawn and the symptoms disappeared.

no clinical investigations of Laetrile's effectiveness, published or otherwise, which are even arguably adequate and well controlled" (Pet. App. 93a-94a). Case reports of physicians who used Laetrile in their practices were anecdotal and otherwise lacking in scientific control and detail (Pet. App. 100a-108a). The Commissioner also evaluated reports of tests in laboratory animals (Pet. App. 114a-126a). He found that these tests failed to show that Laetrile produces anticancer activity in such animals (Pet. App. 126a). Experts from leading medical schools and cancer research and treatment centers (see *id.* at 126a-149a) testified that there is no laboratory or clinical evidence available to support a conclusion that Laetrile is effective, and stated that they could not recognize Laetrile as effective in the absence of such evidence (Pet. App. 126a-149a).

Since the evidence established that Laetrile was not generally recognized by experts as safe and effective for its suggested use as an anticancer drug, the Commissioner concluded that it was a "new drug" under the Act (Pet. App. 163a). It followed that distribution of the drug prior to premarketing approval by the FDA would be unlawful, unless the drug qualified for exempt status under the 1938 or 1962 grandfather provision (*ibid.*).

3. Drugs that were subject to the Pure Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768, and that continue to bear identical labeling concerning conditions of use, are exempted from the "new drug" provisions of the Federal Food, Drug and Cosmetic Act

by Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1). The record evidence before the Commissioner included uncorroborated reports about the use in past centuries of substances claimed to be related to amygdalin or Laetrile (Pet. App. 167a-169a). It also included reports of experiments, beginning in the 1920's, in which Dr. Ernst Krebs, Sr., developed a drug he called "Sarcarcinase"—a drug demonstrably different in chemical structure from drugs now known as Laetrile (Pet. App. 169a-178a, 70a-73a). On the basis of all the evidence, the Commissioner concluded that not only was the record devoid of proof that "Laetrile was used and labeled before 1938 in a manner identical to its present use and labeling," but that the record affirmatively showed "that present day Laetrile was not developed until after 1938" (Pet. App. 178a-179a). He accordingly found that Laetrile does not qualify for exemption under the 1938 grandfather clause (*ibid.*).

4. The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789, redefined a "new drug" as one not generally recognized as both safe and effective. Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1).[9] However, Section 107(c)(4) of the 1962 Drug Amendments, Pub. L. No. 87-781, 76 Stat. 789 (page 3, note 2, *supra*), exempts any drug as to which it is shown: (1) that the same drug, by chemical composition, was used or sold in the United States on October 9, 1962; (2) that the 1962 drug was

[9] Section 201(p) as it read prior to its amendment in 1962 is set forth at Pet. App. 180a.

commercially available at that time; (3) that the 1962 drug was at that time generally recognized by experts as safe for its intended use (and thus was not a "new drug" under the 1938 Act); (4) that the present labeling is the same as the labeling on the drug as sold on October 9, 1962;[10] and (5) that the 1962 drug was not then covered by an effective NDA under the 1938 Act (Pet. App. 179a-181a).

The Commissioner found that Laetrile failed to satisfy four of the five 1962 grandfather requirements.[11] First, the drug in use on the 1962 grandfather date and the Laetrile drugs presently in use did not have an identical composition. The composition of substances referred to as Laetrile varied, and "any drug in use on October 9, 1962 was different in composition from Laetrile as used, or proposed to be used, today" (Pet. App. 187a). Second, the use of Laetrile on the grandfather date was investigational, not commercial, because it was then used only to determine its safety and effectiveness as a cancer treatment (Pet. App. 187a-190a). Third, Laetrile could not be considered to have been generally recognized as safe on October 9, 1962, because experts were largely unfamiliar with the drug, lacked information about its composition and labeled conditions of use, and, in the absence of any published literature regarding safety and effectiveness, would have had no scientific basis on which to recognize the drug as safe (Pet. App. 200a-211a). Fourth, the Commissioner determined that no labeling was described or submitted for Laetrile as a product in use on October 9, 1962, and that even if labeling in a new drug application submitted on October 3, 1962 (see page 8, note 7, *supra*) were viewed as pre-grandfather date labeling, it was not the same as the subsequent labeling and suggested conditions of use (Pet. App. 191a-199a).[12]

[10] The term "labeling" means all written, printed, or graphic matter on or accompanying the drug. 21 U.S.C. 321(m). See *Kordel* v. *United States*, 335 U.S. 345 (1948); *United States* v. *Urbuteit*, 335 U.S. 355 (1948).

[11] The requirement satisfied was that Laetrile was not covered by an effective new drug application on the 1962 grandfather date (Pet. App. 180a).

C. The District Court's Decision After Remand

The district court sustained the Commissioner's finding that Laetrile is a new drug because it is not generally recognized as safe and effective (Pet. App. 19a-22a). The court also left undisturbed the Commissioner's denial of an exemption under the 1938 grandfather clause (Pet. App. 35a). The court concluded, however, that Laetrile qualified for exemption under the 1962 grandfather clause, and it set aside each of the Commissioner's factual findings on this issue (Pet. App. 25a-34a).

[12] The Commissioner relied on a variety of sources to determine how Laetrile was labeled (Pet. App. 191a-199a). Evidence of record demonstrated a wide variance in the indications, conditions of use, dosage form, and manner of administration for Laetrile both before and after 1962 (*ibid.*). See discussion at pages 49-50, *infra*.

The district court found, first, that Laetrile and amygdalin are the same substance, having the chemical formula that the Commissioner used to describe amygdalin alone (Pet. App. 26a n.17). Second, the court concluded that the commercial use of Laetrile as a pharmaceutical product prior to the 1962 grandfather date was established by the availability of amygdalin from chemical supply houses (Pet. App. 29a-30a n.21). Third, from its review of the record the court concluded that prior to 1962 "Laetrile was generally recognized as safe" (Pet. App. 33a & n.24). And fourth, the court determined that labeling proposed for use on an unmarketed drug for which a new drug application was filed on October 3, 1962, established conditions of use on October 9, 1962, and that the present drug qualified for grandfather status to the extent that it bore the same labeling (Pet. App. 15a n.7) (see page 8, note 7, *supra*).

The court also held that by "denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a (footnote omitted)). This holding incorporated a rejection of the evidence credited by the Commissioner that Laetrile has a known toxicity that has not been adequately investigated (Pet. App. 157a-162a, 254a-257a; compare Pet. App. 30a-31a & n.23, and 33a n.24), and a rejection of the Commissioner's factual findings, based on that evidence, that Laetrile is not generally recognized among experts as safe for use in man (Pet. App. 157a).

D. The Decision of the Court of Appeals

The court of appeals, without addressing either the statutory or the constitutional ground on which the district court relied, held "as a matter of law that the 'safety' and 'effectiveness' terms used in the statute have no reasonable application to terminally ill cancer patients" (Pet. App. 3a). The FDA had failed, in the court's view, to advance a standard against which to measure the safety and effectiveness of Laetrile with respect to such patients and had therefore erroneously applied the Act (Pet. App. 6a). The court emphasized that its decision applied only to the intravenous use of Laetrile by terminally ill cancer patients, a group whose members, it concluded, could be identified without difficulty by the certification of a licensed medical practitioner (Pet. App. 5a-6a). The permanent injunction entered by the district court was continued as modified, and the FDA was directed "to promulgate regulations" within the circuit court's guidelines "as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered" (Pet. App. 7a).

SUMMARY OF ARGUMENT

I

The Federal Food, Drug, and Cosmetic Act defines a "new drug" as one not generally recognized by qualified experts as safe and effective for its recommended use. 21 U.S.C. 321(p)(1). The Act provides that "[n]o person shall introduce or deliver for in-

troduction into interstate commerce any new drug * * *" unless a new drug application is effective for that drug, and requires that before a new drug application is approved the drug must be proved to be safe and effective. 21 U.S.C. 355(a), (d). In holding that the safety and effectiveness requirements of the Act do not apply to drugs intended for use by the "terminally ill," the court of appeals has disregarded all relevant guides to statutory construction, including the language of the Act, the purpose it embodies, and the interpretation consistently and reasonably placed on it by the agency charged with enforcing it.

The Act provides certain express exceptions from its safety and effectiveness requirements, but there is no exception for drugs to be used by the "terminally ill." The legislative histories of both the 1938 Act, in which the safety requirement was imposed, and the 1962 amendments, in which the effectiveness requirement was imposed, indicate that Congress specifically intended to make these requirements applicable to drugs for the treatment of cancer, including cancer in its last stages. The Food and Drug Administration, in enforcing both the safety and effectiveness requirements, has never made an exception for drugs to be administered to the terminally ill, and Congress has indicated its acquiescence in this administrative construction.

The Act's standards of safety and effectiveness are not meaningless as applied to drugs to be used by patients who are "terminally ill" with cancer. In the first place, the Commissioner reasonably found that

there is no reliable means of identifying that class of patients, except in retrospect; hence any group so identified can be expected to include some patients who will respond positively to conventional cancer therapies, and for these patients the Act's standards are surely applicable. But even for those who are indeed beyond cure, the standards have meaning. A drug is "unsafe" for such patients, as for anyone else, if it poses risks of shortening life expectancy or aggravating symptoms that are not outweighed by potential benefits of prolonging life, improving health, or ameliorating pain. A drug is "ineffective" for such patients, as for anyone else, if it does not produce the effects of prolonged life expectancy, improved health, or reduced pain that are claimed for it.

The "terminally ill" have as much interest as the general public in the protection that Congress has sought to provide against drugs that are not both safe and effective. Indeed, as the Commissioner noted, the vulnerable psychological state of cancer patients may make them particularly susceptible to unfounded claims and thus create a special need for protection from ineffective drugs. The court of appeals, in holding the statutory standards inapplicable to the "terminally ill," has substituted its judgment for that of Congress and the Commissioner. And although the present case involves only the use of Laetrile under designated conditions, the reasoning of the court of appeals would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective,

thereby impeding if not preventing him from discharging his statutory responsibility to keep unproven drugs out of the marketplace.

II

The 1962 amendments to the Federal Food, Drug, and Cosmetic Act include a grandfather clause that permits the continued marketing—without compliance with the effectiveness requirement established by those amendments—of certain established drugs that were being lawfully marketed in 1962 on the basis of general recognition that they were safe for their recommended uses. The Commissioner found that Laetrile does not qualify for exemption under the 1962 grandfather clause because it fails to meet four of the five requirements for such exemption. The district court reversed the Commissioner's findings and held that Laetrile is exempt under the 1962 grandfather clause. This was error.

Those seeking to qualify a drug for exemption under the 1962 grandfather clause must establish: (1) that the present drug is chemically identical to a drug in existence on the grandfather date in 1962; (2) that the drug was commercially available in 1962; (3) that the drug was at that time generally recognized by experts as safe for its intended use; (4) that the present labeling for the drug is the same as the labeling used for it in 1962; and (5) that the drug was not covered in 1962 by an effective new drug application under the 1938 Act.

Those now seeking to qualify Laetrile under the 1962 grandfather clause do not claim to have marketed the drug commercially on or before the 1962 grandfather date, and therefore lack the reliance interest that the clause is designed to protect. What is more important, the record amply supports the Commissioner's findings that the proponents of Laetrile failed to meet all but the last of the five requirements, and therefore failed to show that Laetrile qualifies for the exemption. Because the Commissioner's findings are supported by substantial evidence and are not arbitrary or capricious, they are entitled to stand. *Citizens to Preserve Overton Park* v. *Volpe*, 401 U.S. 402, 413-414 (1971). The district court's contrary conclusion, reached by an improper reweighing of the scientific evidence, is erroneous and does not provide a ground for sustaining the judgment of the court of appeals.

III

The district court held that "[b]y denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a; footnote omitted). This holding also is erroneous and affords no ground for affirming the decision of the court of appeals.

1. The district court's holding is premised on its unwarranted belief, contrary to the well-supported findings of the Commissioner, that Laetrile has been shown to be nontoxic. The court reached its conclusion by an improper reweighing of the record evidence. It relied heavily on the anecdotal experiences

of a handful of Laetrile practitioners and discounted the testimony of experts, credited by the Commissioner, which indicated that Laetrile is toxic in its oral form and that it has not been adequately tested for toxicity in any form.

2. Even if Laetrile were not toxic, there is no constitutional right to take any particular drug or class of drugs for medical purposes. The assertion of such a right challenges not only the Commissioner's ruling in this case but the Federal Food, Drug, and Cosmetic Act itself, as well as the centuries-old Anglo-American tradition of government protection of the public from foods and drugs that are unsafe, worthless, or fraudulent.

The district court perceived the asserted right as included within the constitutional right of privacy recognized by decisions of this Court beginning with *Griswold* v. *Connecticut*, 381 U.S. 479 (1965). In particular, the district court relied on a line of cases that this Court has characterized as protecting the individual's interest in making independent decisions in "matters relating to marriage, procreation, contraception, family relationships, and child rearing and education." *Whalen* v. *Roe*, 429 U.S. 589, 600 n.26 (1977), quoting *Paul* v. *Davis*, 424 U.S. 693, 713 (1976).

A right of caring for one's health by obtaining a particular drug without government hindrance does not fall within any of those categories and does not involve the kind of decision with which those cases were concerned. On the contrary, the Court's reason-

ing in that line of cases leads to rejection of the constitutional claim here. In *Roe* v. *Wade*, 410 U.S. 113 (1973), and other cases involving abortion and contraception laws, where the Court has upheld a right of privacy in matters relating to marriage and procreation, it has at the same time made it quite clear that that right may be restricted in the interest of protecting the health of the persons concerned. This recognition is inconsistent with the claimed constitutional right of access to drugs that fail to meet the requirements of a statutory system aimed at protecting the public health by assuring that marketed drugs are safe and effective for their intended uses.

The conclusion that the Constitution guarantees no right of access to ineffective drugs draws further support from this Court's opinion in *Whalen* v. *Roe*, *supra*, 429 U.S. at 603. The Court there stated that a state "no doubt could prohibit entirely" the use of the class of drugs involved in that case—drugs that "have accepted uses in the amelioration of pain and in the treatment of [various diseases]" but that are subject to abuse (*id.* at 593 n.8). It follows a fortiori that the government may prohibit interstate commerce in a drug that has no recognized medical use for the life-threatening disease for which it is recommended, and that has a potential for harming, at the least, those patients who are deterred by the drug's availability from seeking effective treatment.

The logic of the constitutional claim asserted here goes well beyond the contours of this case. Recognition of the claim would make it difficult, if not im-

possible, for Congress and the Commissioner to enforce the safety and efficacy requirements of the Act with respect to any drug that a court might conclude is nontoxic, that a physician somewhere is willing to prescribe, and that some individual wishes to take. And recognition of the constitutional claim would impede the states as well as the federal government from enforcing health-related regulation of drugs.

3. Even if the constitutional right of privacy did include a right to take particular drugs for medical purposes, any such right to use Laetrile is outweighed by compelling governmental interests in protecting the public health.

Specifically, the government has a compelling interest (1) in maintaining the confidence of the public and the medical profession in the safety and efficacy of the marketed drug supply; (2) in seeing that persons suffering from cancer, both in its early and later stages, are not deterred by the availability of an unproven drug such as Laetrile from seeking timely treatment by therapies of proven effectiveness; and (3) in seeing that cancer patients and their families are not defrauded by the promotion of costly but ineffective drugs.

Prohibiting the importation and interstate distribution of Laetrile is a reasonable means of effectuating these interests—even where only the availability of Laetrile to patients classified as "terminally ill" is concerned, and even assuming that patients in this class are beyond the help of conventional therapies. Government acquiescence in even limited availability of Laetrile may suggest to cancer patients generally that the drug has some value. There is a real danger, illustrated by incidents of record in this case, that drugs ostensibly provided for those classified as terminally ill will be made available to other patients whose cancers are demonstrably in earlier, curable stages.

ARGUMENT

I

THE SAFETY AND EFFECTIVENESS REQUIREMENTS OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT APPLY TO DRUGS INTENDED FOR USE BY THE TERMINALLY ILL

The court of appeals cited no authority of any kind for its conclusion that the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act do not apply to Laetrile when it is obtained for intravenous administration by physicians to "terminally ill" cancer patients.[13] The court's conclusion is contrary to the language of the Act, the legislative purpose it embodies, and the consistent and reasonable interpretation placed on the Act by the agency charged with enforcing it. The conclusion is also unsupported by case law or other authority.

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[13] We use the term "terminally ill" because that is the term used by the court of appeals to describe the group of patients entitled under its order to use Laetrile despite the drug's noncompliance with the safety and effectiveness requirements of the Act. However, we are not certain of the meaning of the term, since the court did not define it, and as we note below (page 30), there is no reliable means of identifying such a group.

A. We start with some familiar principles. When the purpose of a congressional enactment "has been effected by plain and unambiguous language, and the act is within the power of Congress, the only duty of the courts is to give it effect according to its terms." *United States* v. *Lexington Mill Co.*, 232 U.S. 399, 409 (1914); see *TVA* v. *Hill*, 437 U.S. 153, 173, 187, 193-195 (1978). The only circumstance in which a statute may properly be construed to mean something other than what it plainly says is where a literal reading " 'would lead to absurb results * * * or would thwart the obvious purpose of the statute.' " *Trans Alaska Pipeline Rate Case*, 436 U.S. 631, 643 (1978), quoting *Commissioner* v. *Brown*, 380 U.S. 563, 571 (1965). In particular, implied exceptions to clearly delineated statutory coverage are disfavored and will not be found unless they are essential to avoiding an obvious inconsistency with the statutory scheme. *United States* v. *Key*, 397 U.S. 322, 324-325 (1970); see *TVA* v. *Hill*, *supra*, 437 U.S. at 188; 2A *Sutherland on Statutes and Statutory Construction* § 47.11 at 90 (4th ed. C. Sands 1973).

When the proper construction of a statute is in doubt, there is a special principle applicable to legislation such as food and drug laws. It is "the well-accepted principle that remedial legislation such as the Food, Drug, and Cosmetic Act is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health * * *." *United States* v. *An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969). But there is no need to invoke

that principle when the "overriding purpose" of protecting the public health can be achieved simply by giving effect to the statute according to its plain terms. *United States* v. *Lexington Mill Co.*, *supra*, 232 U.S. at 409.

In determining a statute's purpose, courts properly look not only to the language and the legislative history of the Act, but also to the views of the agency charged with administering the Act. *Bayside Enterprises, Inc.* v. *NLRB*, 429 U.S. 298, 304 (1977); *Red Lion Broadcasting Co.* v. *FCC*, 395 U.S. 367, 381 (1969); *Udall* v. *Tallman*, 380 U.S. 1, 16 (1965). Those views are entitled to special weight when Congress, in amending the Act, has declined to alter it so as to defeat the administrative construction. *Red Lion Broadcasting Co.* v. *FCC*, *supra*, 395 U.S. at 381; *Zemel* v. *Rusk*, 381 U.S. 1, 11-12 (1965).

B. Here, the statutory language is clear. It provides (Section 505(a) of the Act, 21 U.S.C. 355(a)) that

> No person shall introduce or deliver for introduction into interstate commerce any new drug * * *

unless a new drug application is effective for that drug; and it defines "new drug" (Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1)) as

> [a]ny drug * * * not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling * * *.

The statute further provides that before a new drug application is approved, the drug must be proved to be safe and effective. It must be proved safe through "adequate tests by all methods reasonably applicable," and it must be proved effective by "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved * * *" (Section 505(d) of the Act, 21 U.S.C. 355(d).

The statute does provide certain exemptions from these premarketing clearance procedures. Three categories of drugs are exempted: (1) grandfathered drugs; (2) drugs that are not "new" —*i.e.*, that experts generally recognize as safe and effective on the basis of scientific investigations meeting the requirements of Section 505(d) (see *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629-630 (1973)); and (3) drugs that are intended solely for investigational use by qualified investigators and that meet other requirements specified in regulations authorized by the Act (Section 505(i), 21 U.S.C. 355(i)).

But these exemptions are specific and limited. The Act provides no exemption for drugs intended for the "terminally ill" or for any other group of patients. The language by which Congress has required that drugs be safe and effective before they may be distributed in interstate commerce is inclusive.

To give effect to the Act as written would in no respect offend the congressional purpose. There is no

indication from any source that Congress did not intend to protect the public health by ensuring, as the language of the Act requires, that all available and nonexempt drugs are both safe and effective for their intended uses. On the contrary, the legislative history of both the 1938 Act and the 1962 amendments indicates that Congress intended to make the safety and effectiveness requirements applicable to drugs intended for use by the terminally ill in particular.

In its deliberations preceding enactment of the 1938 Act, in which the preclearance requirement of establishing the safety of new drugs was imposed, Congress expressed its concern over drugs purporting to treat cancer. See, *e.g.*, 79 Cong. Rec. 5023 (1935) (remarks of Sen. Copeland, sponsor of the Act); 83 Cong. Rec. 7786-7787, 7789 (1938) (remarks of Reps. Phillips and Lea). See also S. 2000, 73d Cong., 2d Sess. § 9(c) (1934), reprinted in C. Dunn, *Federal Food, Drug and Cosmetic Act* 58 (1938); S. 5, 75th Cong., 1st Sess. § 3(4) (1937), reprinted in Dunn, *supra*, at 639. And there was no suggestion that cancer drugs would be subject to the Act only when they were to be administered to patients whose cancers were "curable."

During the proceedings leading to the 1962 amendments, Congress recognized that the Act would apply to experimental drugs used to treat "cancer in its last stages." 108 Cong. Rec. 17399 (1962) (remarks of Sen. Kefauver, chairman of the committee reporting the bill). Senator Eastland, another proponent of the bill, assumed that drugs administered for

"fatal diseases, such as cancer," would be subject to the Act's requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering. 108 Cong. Rec. 17401 (1962).

In accord with the statutory language and the evident congressional purpose, the FDA, in enforcing the safety requirements in Section 505(d) of the Act before 1962 and in enforcing both the safety and the effectiveness requirements since 1962, has never made an exception for new drugs that are to be administered to the terminally ill. Had Congress disapproved of this consistent course of administrative action, it could have amended the Act accordingly when it enacted the 1962 amendments or at any time since.[14]

Nor is there support in the case law for the construction given the Act by the court of appeals here. The only prior federal appellate decision[15] that considered the interests of the terminally ill in obtaining access to an anticancer drug was *Rutherford* v.

[14] In enacting the 1962 amendments, which adopted the effectiveness requirement for all new drugs, Congress specifically approved the FDA's longstanding policy of requiring a demonstration of effectiveness as part of the safety requirement for drugs used in the treatment of life-threatening diseases. S. Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 15 (1962); H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). See pages 47-48, *infra*.

[15] Some district courts have granted preliminary relief permitting cancer patients diagnosed as terminally ill to receive supplies of Laetrile through interstate commerce (see page 50, note 35, *infra*), but none has held the Act's safety and effectiveness standards inapplicable to drugs for the terminally ill.

American Medical Association, 379 F.2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043 (1968). The court of appeals there implicitly accepted the proposition that the safety and efficacy requirements of the Act apply to drugs intended for use by the terminally ill.[16]

C. The court of appeals ruled that the Act's standards of safety and effectiveness have "no meaning," and hence "no application," with respect to a drug intended for use by cancer patients who are "terminally ill" (Pet. App. 5a-7a). This ruling is erroneous for several reasons.

1. First, and most fundamental, the court substituted its view for that of Congress with respect to what constitutes a reasonable and appropriate regulatory scheme. Where the congressional scheme requires proof of the safety and effectiveness of all new drugs, except those categories of drugs that Congress expressly exempted, the court created a new exemption for drugs intended for a category of patients. It is not for a court to add exemptions to those that Con-

[16] In that case a doctor and "hopeless" cancer patients (379 F.2d at 642) sought to enjoin the FDA and others from interfering with the distribution of another drug allegedly effective in the treatment of cancer. The court held that "initial approval or exemption of a drug is within the primary jurisdiction of the FDA." *Id.* at 643. In the absence of a good faith application to the agency for such approval or exemption, the court lacked jurisdiction to review the refusal to permit the marketing of the drug. *Ibid.* The opinion notes that Section 355 of the Act establishes a procedure for submitting adequate scientific information about a new drug to the FDA to "permit an intelligent assessment of its safety and efficacy" (*ibid.*).

gres provided (*TVA* v. *Hill*, *supra*, 437 U.S. at 188), or to let its own "individual appraisal of the wisdom or unwisdom of a particular course consciously selected by the Congress" be its guide in interpreting a statute (*id.* at 194).

2. In creating the exception for the "terminally ill"—a term it made no attempt to define—the court of appeals also disregarded the judgment of the Commissioner, supported by expert medical testimony, that there is no objectively identifiable group of cancer patients comprising such a class, except in retrospect (Pet. App. 98a, 267a-268a). Cancer in individuals frequently takes an unpredictable course; there may be unexpected and unexplainable remissions, and one person may differ from another in his response to a particular mode of therapy (Pet. App. 98a, 268a). As the Commissioner also found, again with the support of expert testimony, even if one could reliably distinguish between the terminally ill and those who will respond to conventional cancer treatment, it would be virtually impossible, as a practical matter, to restrict the use of Laetrile to the terminally ill (Pet. App. 269a-270a).

Judgments such as these, reflecting an agency's technical expertise supported by substantial record evidence, may not simply be disregarded by the courts. *Ciba Corp.* v. *Weinberger*, 412 U.S. 640, 643-644 (1973); *United States* v. *An Article of Drug . . . Bacto-Unidisk*, *supra*, 394 U.S. at 791-792; *New York* v. *United States*, 331 U.S. 284, 327 (1947). See also *Vermont Yankee Nuclear Power Corp.* v. *Natural Resources Defense Council, Inc.*, 435 U.S. 519, 557-558 (1978).

3. Even if it were appropriate for a court to depart from the plain meaning of legislation and the record-supported judgment of the expert agency in order to avoid "unreasonable" results, the decision of the court of appeals would be improper because there is no unreasonable result to avoid. There is nothing unreasonable in protecting patients diagnosed as "terminally ill" from unsafe or ineffective drugs, and the court was wrong in thinking that the Act's standards of safety and effectiveness have no meaningful application to drugs intended for use by such patients.[17]

A drug is "safe," within the meaning of the Act, if the benefits expected to be achieved through its administration outweigh the costs or risks incurred.[18]

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[17] We assume arguendo at this point that the "terminally ill" can be reliably identified. In fact, as we have noted, they cannot be, and any class of patients so certified may be expected to include some for whom conventional therapies may succeed, at least in significantly prolonging life. The Act's standards of safety and effectiveness are surely applicable to such patients, even if one accepts the view of the court of appeals that they are not applicable to patients whose illness is truly "terminal."

[18] "[A] drug is safe when the expected therapeutic gain justifies the risk entailed in using it * * *." Dr. Theodore G. Klumpp, Chief, Drug Division, FDA, June 23, 1941, Food Drug Cos. L. Rep. (CCH) ¶ 71,053.59, at 71,063; see also M. White, *"Administrative Procedure and Practice in the Department of Agriculture under the Federal Food, Drug, and Cosmetic Act of 1938"* 95 (1940), reprinted in H. Toulmin, Jr., *A Treatise on the Law of Food, Drugs and Cosmetics* 635 (1942).

No drug is completely "safe" in the lay person's sense of the word, since every drug—aspirin not excepted—involves risks.[19] Thus, safety has the same meaning with respect to drugs intended for terminally ill cancer patients as it does generally. A drug that may shorten a terminally ill patient's life expectancy or cause other physical harm, without a more-than-compensating potential for benefiting the patient, is unsafe. The judgment of the court of appeals, limiting its authorized use of Laetrile by requiring that the drug be administered only by a licensed physician and only through intravenous injection (Pet. App. 8a-9a), betrays the court's own recognition that considerations of safety are applicable to regulation of the use of drugs by the terminally ill.[20]

"Effectiveness" under the Act requires the sponsor of a drug to provide substantial evidence that the drug produces the effects claimed for it. Section 505 (d), 21 U.S.C. 355(d).[21] Effectiveness does not, as

[19] See L. Goodman & A. Gilman, *The Pharmacological Basis of Therapeutics* 325-339 (5th ed. 1975).

[20] The Act itself distinguishes between drugs that are safe for self-administration and those that are safe only when administered by a physician. See, *e.g.*, Section 503(b) of the Act, 21 U.S.C. 353(b). The court's restriction on the method of administration (and its denial of respondents' petition requesting an amendment of the judgment to permit the use of Laetrile in oral form) is unexplained, but may reflect the court's acknowledgement of record evidence indicating that Laetrile taken orally is toxic (Pet. App. 157a-162a).

[21] There is a relationship, of course, between drug safety and efficacy. As Senator Kefauver stated when introducing the bill that became the 1962 amendments, "[a]n otherwise completely safe drug can be dangerous to the patient if it does not have the therapeutic effect in use which it is represented to have." 107 Cong. Rec. 5640 (1961).

the court of appeals implied (Pet. App. 6a), necessarily connote curative properties.[22] Thus, for a terminally ill patient, as for anyone else, a drug that fails, by objective measures, to fulfill its sponsor's claim of increased life expectancy, ameliorated physical condition, or reduced pain is ineffective.

The terminally ill, whether victims of cancer or of any other disease, have as much interest as the general public in protection from drugs that are not both safe and effective. To exempt Laetrile from the Act's requirements when used by terminally ill cancer patients would, as the Commissioner concluded (Pet. App. 270a):

> * * * lead to needless deaths and suffering among (1) patients characterized as "terminal" who could actually be helped by legitimate therapy and (2) patients clearly susceptible to the benefits of legitimate therapy who would be misled as to Laetrile's utility by the limited approval program or who would be able to obtain the drug through the inevitable leakage in any system set up to administer such a program.

Moreover, as the Commissioner noted (Pet. App. 224a-230a), the vulnerable psychological state of can-

[22] Neither does it involve consideration of the relative effectiveness of one drug compared with another, or require proof of unanimous scientific opinion. S.Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 56-58 (1962) (views of Sen. Dirksen and Sen. Hruska); S. Rep. No. 1744 (Part 2), 87th Cong., 2d Sess. 6 (1962).

cer patients may make them particularly susceptible to unfounded claims and thus create a special need for protection from ineffective drugs.[23]

D. In sum, the decision of the court of appeals represents an improper substitution of its own judgment for that of Congress and the Commissioner, who have determined that an exemption from the Act's safety and effectiveness requirements for drugs used by cancer patients characterized as "terminally ill" is neither appropriate nor feasible. The court's decision seriously limits the Commissioner's power to protect the public from unsafe and ineffective drugs.

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[23] If the decision of the court of appeals was animated by an unarticulated view that Laetrile may be the only hope available for terminally ill cancer patients who are not aided by conventional therapy, that view was misconceived. Many different experimental cancer drugs are available. Under Section 505(i) of the Act, 21 U.S.C. 355(i), exemptions from the premarketing requirements of Section 505(d) may be given for drugs intended solely for investigational use, if preclinical tests of the drug (including tests on animals) are "adequate to justify the proposed clinical testing" and if certain other requirements as to recordkeeping and informed consent are met. FDA records show that at the present time there are more than 300 oncologic drugs under clinical investigation under exemptions granted pursuant to 21 U.S.C. 355(i). All of these drugs are available, at authorized institutions, for use by critically ill patients.

We are informed by the National Cancer Institute (NCI) that during 1977 some 63,000 patients were receiving such drugs in NCI treatment programs or were being evaluated in follow-up programs conducted by NCI's extramural clinical trials division. NCI also reports that in 1977 approximately 12,000 cancer patients were in similar Veterans Administration treatment or follow-up programs. The same year another 22,800 cancer patients were treated with investigational drugs in programs directed by independent investigators under NCI auspices. In addition to conducting clinical trials on promising drugs, NCI screens from 15,000 to 30,000 natural and synthetic compounds a year to determine their potential anti-cancer activity; between 1956 and 1976, over 475,000 compounds were evaluated. See Division of Cancer Treatment, National Cancer Institute, *Treatment Linear Assay* 3 (December 1976).

An application by NCI to undertake clinical testing of Laetrile is pending before the Commissioner.

Although the present ruling is limited to the intravenous use of Laetrile by terminally ill cancer patients, the court's analysis of the Act would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective. See Comment, *Laetrile: Statutory and Constitutional Limitations on the Regulation of Ineffective Drugs*, 127 U. Pa. L. Rev. 233, 255 (1978). The decision thus would make it difficult, if not impossible, for the Commissioner to discharge his statutory responsibility to keep unproven drugs out of the marketplace.[24]

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[24] The court directed the FDA to "promulgate regulations * * * as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered" (Pet. App. 7a). It is difficult to see how the FDA could comply. In the absence of adequate data, there is no basis on which to label Laetrile in the manner required by Section 502 (21 U.S.C. 352). Directions for drug use—including indications, contraindications, dosages, routes of administration, warnings, side effects, and necessary collateral measures—are premised on a body of data derived from extensive testing. As the Commissioner found, such data do not exist for Laetrile (Pet. App. 93a-211a, 270a-272a); neither court below disagreed with this conclusion. Without such testing data, the drug cannot be labeled for any use. Any

II

LAETRILE IS A NEW DRUG THAT IS NOT EXEMPTED FROM THE PREMARKETING CLEARANCE REQUIREMENTS OF THE ACT BY OPERATION OF THE 1962 GRANDFATHER CLAUSE

1. The Commission found (a) that Laetrile is a new drug subject to the premarketing clearance requirements of the Act because it is not generally recognized by qualified experts as safe and effective (Pet. App. 88a-162a), and (b) that Laetrile does not qualify for exemption under the 1962 grandfather clause because it fails to meet four of the five requirements for such exemption (Pet. App. 179a-211a). The district court sustained the former finding (Pet. App. 22a) but rejected the latter (Pet. App. 25a-27a).[25] In rejecting the Commissioner's grandfather clause determination, the district court

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suggestion in labeling that the drug may be safely or effectively used would misbrand the drug in violation of Sections 502(a) and 505(d)(6) (21 U.S.C. 352(a) and 355(d)(6)). Effective regulations authorizing an affidavit system similar to that now maintained by order of the district court (A. 5-6, 57-58) (see page 5, note 6, *supra*) would also be difficult to devise, since there have been indications that the current system results in distribution of Laetrile to persons not within the certified class of terminally ill cancer patients (see page 74, *infra*).

[25] As noted above (page 11), the Commissioner also concluded that Laetrile is not entitled to exemption under the 1938 grandfather clause (included in Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1)), and the district court did not overturn this conclusion. Respondents did not raise this issue in the court of appeals

misunderstood the purpose of the clause and improperly reversed the Commissioner's factual findings with regard to the chemical composition of the 1962 drug, its safety reputation among medical experts, its commercial availability, and its labeling.

The 1962 grandfather clause, Pub. L. No. 87-781, Section 107(c)(4), 76 Stat. 789, provides:

> In the case of any drug which, on [October 9, 1962] the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective [new drug] application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

The purpose of grandfather clauses generally is to protect the reliance interests of those whose previously lawful investments or means of earning income would be adversely affected by application of new legislation. See, *e.g.*, *New Orleans* v. *Dukes*, 427 U.S. 297, 305 (1976). The purpose of this grandfather clause is to permit the continued marketing—without compliance with the new effectiveness requirement established by the 1962 amendments—of certain established drugs that were lawfully marketed without an approved new drug application in 1962 because they were generally recognized as safe for

their labeled uses. *USV Pharmaceutical Corp.* v. *Weinberger*, 412 U.S. 655, 663-664 (1973). Drugs lawfully marketed as "new drugs" in 1962 were not exempted from the effectiveness requirement imposed by the 1962 amendments, but were given a two-year grace period in which to comply. *Ibid.*[26] A fortiori, Congress did not intend by the 1962 grandfather clause to establish criteria that a subsequently introduced product, not marketed in 1962, could meet in order to avoid having to provide the proof of effectiveness required by the 1962 amendments.

Laetrile was not being marketed commercially on October 9, 1962, and has not been continuously marketed in the same composition and with the same labeling since that date. The present proponents of Laetrile, moreover, do not claim that *they* were marketing the drug in 1962.[27] They thus do not seek

[26] Thus, a drug that *was* "covered by an effective [new drug] application" on October 9, 1962, was thereby excluded from the grandfather clause (see subpart (C), quoted at page 37, *supra*); but, under another section of the 1962 amendments (Section 107(c)(3), 76 Stat. 788-789), such a drug was allowed to continue being marketed for two years. This was to give manufacturers of drugs covered by NDA's a reasonable opportunity to generate effectiveness data in order to qualify the drugs for marketing under the new amendments.

[27] Participation in the proceeding before the Commissioner was not limited to the parties to the district court suit and their designated witnesses. All who wished to make oral presentations, written submissions, or both, were permitted to do so, whether or not they had any connection with the court action. (Pet. App. 48a-51a). Those who submitted presentations aimed at supporting the claim that Laetrile should be

protection of interests enjoyed by manufacturers in 1962 and maintained to the present. Rather, they seek to justify an essentially new marketing venture under the mantle of various pre-1962 drugs. Even if their claim to satisfy the requirements of the 1962 grandfather clause were more colorable than it is, it would distort the purpose of the clause to extend its protection to them. It would also offend the principle that such a clause, as a restriction on the scope of remedial legislation and a limitation of the protection afforded the public against ineffective drugs, should be narrowly construed. *USV Pharmaceutical Corp.* v. *Weinberger*, *supra*, 412 U.S. at 667; *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 633-634; *Durovic* v. *Richardson*, 479 F.2d 242, 250 n.6 (7th Cir.), cert. denied, 414 U.S. 944 (1973); *United States* v. *An Article of Drug . . . "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), cert. denied, 412 U.S. 938 (1973).

2. Although the 1962 grandfather clause has three subparts designated (A), (B), and (C), it essentially sets out, as noted above (page 11-12, *supra*), five factual propositions that must be established as the

available for distribution through interstate commerce included cancer patients (Pet. App. 231a, 235a), persons associated with the development of Laetrile as a drug recommended for the treatment of cancer (Pet. App. 50a, 79a-88a), and persons who dispense the drug through clinics (Pet. App. 237a). The Commissioner considered all views submitted for the record (Pet. App. 50a-51a). Hence our references to "proponents" of Laetrile are not limited to respondents and their witnesses and representatives.

basis for exempting a drug from the effectiveness requirements imposed by the 1962 amendments. Failure to prove any one of the five makes the exemption inapplicable. *United States* v. *An Article of Drug . . . "Bentex Ulcerine," supra,* 469 F.2d at 878. Thus the proponents of Laetrile had the burden of proving: (1) that present-day Laetrile is chemically identical to a drug in existence on October 9, 1962; (2) that the drug was then commercially available; (3) that the drug was at that time generally recognized by experts as safe for its intended use (and thus was not a "new drug" under the 1938 Act); (4) that present labeling (including directions for use) is the same as the labeling on the drug as sold on October 9, 1962; and (5) that the drug was not then covered by an effective NDA under the 1938 Act.

The Commissioner found that the proponents of Laetrile had failed to meet all but the last of these requirements and that Laetrile therefore is not exempt under the 1962 grandfather clause. The district court reached a contrary conclusion by reweighing the scientific evidence and substituting its own findings for those of the Commissioner; the court did not determine, under the appropriate standard of judicial review of administrative findings, that the Commissioner's decision was arbitrary and capricious or was not supported by substantial evidence. See *Citizens to Preserve Overton Park* v. *Volpe,* 401 U.S. 402, 413-414 (1971); *Illinois Central R.R.* v. *Norfolk & Western Ry.,* 385 U.S. 57, 65-66 (1966); *Consolo* v. *FMC,* 383 U.S. 607, 618-620 (1966).

a. *Composition.* First, the Commissioner properly found that the proponents of Laetrile had failed to demonstrate that the drug or drugs now sold as Laetrile have the same composition as a drug sold on October 9, 1962. As the Commissioner noted, the fact that a drug used or sold on October 9, 1962, has some ingredients in common with a drug used or sold today would not establish identity of composition sufficient to satisfy the requirements of the grandfather clause (Pet. App. 182a-183a). A change in any of the ingredients, including inactive ingredients, or in the proportion of the ingredients, will make a drug a "new drug." See 21 C.F.R. 310.3(h); *United States* v. *An Article of Drug . . . "Entrol-C Medicated,"* 513 F.2d 1127, 1130 n.7 (9th Cir. 1975).

The Commissioner found that the composition of the different substances referred to as Laetrile both before and after 1962 varied considerably, and that the 1962 formulations differed from the formulations currently in use (Pet. App. 182a-187a).[28] Consequently, he determined that the proponents of Laetrile had failed to sustain the burden of showing that either Laetrile or amygdalin as presently constituted was in use on October 9, 1962. *Ibid.*

The district court rejected the Commissioner's findings on this point and found "that Laetrile and Amygdalin are equivalent and have been recognized

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[28] Laboratory analyses of drugs called Laetrile have often revealed both variances from labeled composition and variations in component parts and in the percentage of amygdalin present (Pet. App. 184a-185a).

as such for over 20 years" (Pet. App. 26a n. 17).[29] The court did not identify the quantitative or qualitative composition of any drug sold on October 9, 1962, but relied instead on general references in the record to an identity between Laetrile and amygdalin, none of which was specific as to chemical formulation for any given date.[30] Even if the references cited by the court supported its conclusion, they would not provide an adequate basis for displacing the Commissioner's finding that Laetrile in its present forms was not in use on October 9, 1962,

[29] This conclusion is contrary to that reached by the district court in *United States* v. *Eartheo*, No. CV 78-3602-HP (C.D. Cal. Jan. 24, 1979).

[30] None of the materials cited by the district court (Pet. App. 26a n.17) comes close to establishing the identity of any of the current Laetrile formulations with any drug available in 1962 or before. For example, the court cited and quoted the Commissioner's statement that "Laetrile is the name of a product whose *major component or ingredient* is the chemical amygdalin, * * *" (emphasis supplied). It also cited (*ibid.*) a pamphlet prepared by the American Cancer Society for distribution to the public, a document that can hardly be expected to provide precise information on the formulation of the drug. Frank Rauscher's "Statement Concerning Laetrile" (A. 59-60), contrary to the court's assertion (Pet. App. 26a n.17), does not even mention "amygdalin." Neither the deposition of Dean Burk (A. 67-76), which uses the terms "Laetrile" and "amygdalin" interchangeably, nor the deposition of Raymond Ewell (A. 77-79), attempts to identify a formulation for Laetrile or amygdalin at any specific time. All that Dr. Ewell stated was that "only a few people consume *amygdalin* in its pure form," which is "known popularly as laetrile." Other record references by the district court are similarly irrelevant to the issue of chemical identity.

since the Commissioner's finding is based on substantial evidence of record and is not arbitrary or capricious (Pet. App. 187a). See, *e.g.*, *Citizens to Preserve Overton Park* v. *Volpe*, *supra*, 401 U.S. at 413-414.

b. *Commercial availability.* The district court committed similar error in rejecting the Commissioner's findings on the commercial availability of Laetrile on October 9, 1962. Commercial availability means that the drug has been "openly and readily available and broadly distributed in the ordinary course of business" and that there was no "restriction to investigational use * * *." *Durovic* v. *Richardson*, *supra*, 479 F.2d at 248. Unless a drug was available generally for commercial use on October 9, 1962, the manufacturer lacks the reliance interest recognized by Congress as warranting an exception to the requirement of effectiveness. The administrative record fully supports the Commissioner's conclusions that Laetrile, as of October 9, 1962, was not openly and readily available and was not broadly distributed in the ordinary course of business, but was in fact restricted to investigational use (Pet. App. 187a-190a).[31]

[31] As the Commissioner noted, Dr. Ernst T. Krebs, Sr., a developer of Laetrile, stated in a 1965 affidavit that his shipments of Laetrile from as early as 1926 and up through 1962 "were for investigational use only" (Pet. App. 187a). The conclusion that the use of Laetrile was continuously investigational in nature was reinforced by other evidence. First, in 1952, the FDA collected Laetrile labeling which read in part: "Caution: New drug limited by Federal Law to investigational use" (Pet. App. 189a). Second, on October 3, 1962,

The district court recognized, as did the Commissioner, that investigational use of a drug does not prove commercial availability, and it attempted to rely on other evidence from the record (Pet. App. 29a & n.21). Although the court's opinion states that "[t]he record's whole tenor reasonably establishes the commercial availability of Laetrile (Amygdalin) during the period in question" (Pet. App. 30a n.21), only two submissions are cited. One is an affidavit by Charles Gurchot, Ph.D., which stated that amygdalin was "a purchaseable item in various chemical catalogs published in the United States" (*ibid.*). The other is a letter from N. Schneider of Van, Waters & Rogers, Inc., a chemical supply house dealing in amygdalin (*ibid.*), which simply quoted prices for amygdalin; it did not provide chemical specifications.

Even if it is assumed, contrary to the Commissioner's finding, that present-day Laetrile and amygdalin are chemically identical substances, proof that a chemical supply house was selling the compound amygdalin before 1962 does not establish that a *drug* with that chemical composition was then commercially available. A chemical supply house sells raw chemicals, not pharmaceuticals prepared in dosage forms with labeling for use as drugs. Such a firm would lack a cognizable proprietary interest in the sale of a drug, and there would thus be no reason to permit the firm itself—let alone others having no connection with it—to sell such compounds as drugs after October 9, 1962, without meeting the new standards of the Act.

Ernst T. Krebs, Jr., submitted an NDA for Laetrile (Pet. App. 191a-192a) (describing the drug as approximately 80% amygdalin, *id.* at 185a); since at that time the Act defined a "new drug" as one not generally recognized as safe, the filing of the NDA constituted an acknowledgement by one of its leading proponents that Laetrile was not generally recognized as safe and was restricted to investigational use (see Pet. App. 181a). Third, under the terms of his probation following conviction for selling another unproven drug, Ernst Krebs, Jr., was permitted by court order on June 28, 1962, to ship some Laetrile in interstate commerce for investigational use only (Pet. App. 187a-188a).

c. *Safety.* The 1962 grandfather clause, by its exclusion of drugs that were "new drugs" as defined in Section 201(p) of the pre-existing Act, requires a drug to have been generally recognized as safe under its labeled conditions of use on October 9, 1962.[32] This, in turn, signifies that there must have existed on October 9, 1962, "investigations * * * includ[ing] adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use * * *." Section 505(d)(1) of the Act, 21 U.S.C. 355(d)(1); *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 653 (1973) ("the reach of scientific inquiry under both § 505(d) and under § 201(p) is precisely the same"). Unless data from such tests were available in the scientific literature, there could be no basis for general recognition of safety among experts. *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *supra*; see also, *e.g.*, *United States* v. *41 Cases, More or Less*, 420 F.2d 1126, 1130 (5th Cir. 1970).

[32] Section 201(p), 21 U.S.C. (1958 ed.) 321(p), as it appeared prior to the 1962 amendment, appears at Pet. App. 180a.

The administrative record fully documents the absence in 1962, and today, of any general recognition among qualified experts of Laetrile's safety. Indeed, the record contains substantial evidence (see Pet. App. 201a-208a) indicating that Laetrile was not generally known at all to the community of medical experts on October 9, 1962. Moreover, as noted earlier, because of the pre-1962 variability in the composition of Laetrile, and the varied conditions of use recommended in its labeling, Laetrile could in no event have been generally recognized as a drug whose composition was safe "for use under the conditions prescribed, recommended, or suggested in the labeling" for it. 21 U.S.C. (1958 ed.) 321(p)(1) (Pet. App. 180a).

The Commissioner's finding that Laetrile was not generally recognized by experts as safe on October 9, 1962, did not rest solely on the absence of scientifically developed data indicative of the drug's safety. It was also based on testimony of some of the nation's leading cancer scientists that Laetrile presents significant hazards to persons to whom it is administered (Pet. App. 158a-160a, 162a). For example, Dr. Joseph F. Ross, professor of medicine and Director of the Research Training Program in Hematology and Hematologic Oncology at UCLA (Pet. App. 146a), testified that oral ingestion of Laetrile or amygdalin presents "a definite health hazard" because it "may produce acute cyanide poisoning" (Pet. App. 162a). Even proponents of Laetrile have labeled the drug to warn of the toxic effects of oral administration (Pet. App. 158a).

In determining that Laetrile was generally recognized as safe on October 9, 1962 (Pet. App. 33a), the district court did not address the implications of the lack of any scientific data on the safety of Laetrile on or prior to that date.[33] Instead, contrary to this Court's decisions (*e.g.*, *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *supra*), the district court relied on anecdotal experiences recounted in several submissions from Laetrile proponents (Pet. App. 33a n.24).

The district court compounded this error by holding that no showing of Laetrile's effectiveness as a cancer drug was required in order for it to have been generally recognized as safe on October 9, 1962 (Pet. App. 28a n.18). Congress, when it was considering the 1962 amendments to the Act, recognized that in the case of drugs used for life-threatening diseases, evidence of effectiveness was considered by the FDA to be essential to proof of safety. The Senate Report on the 1962 amendments stated:

> The Food and Drug Administration now requires, in determining whether a "new drug" is safe, a showing as to the drug's effectiveness where the drug is offered for use in the treatment of a life-threatening disease, or where it appears that the "new drug" will occasionally

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[33] The district court did not make any specific findings on this point and cited only a single record reference—which the Commissioner found reasons to discount (Pet. App. 206a-207a)—indicating an affiant's information and belief that "pure amygdalin" has been generally recognized as safe among qualified experts since the 1930's (Pet. App. 33a n.24).

> produce serious toxic or even lethal effects so that only its usefulness would justify the risks involved in its use.

S. Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 15 (1962). The legislative reports make it clear that the amendments were not intended to affect the then-existing authority of the FDA to pursue this practice of considering the effectiveness of a new drug to be used for a life-threatening disease in the context of passing on its safety. *Ibid.*; see also H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). Thus, a lack of general recognition of the effectiveness of a drug intended for treatment of a life-threatening disease on October 9, 1962, means that general recognition of its safety could not have existed. As the Seventh Circuit held in *Durovic* v. *Richardson, supra*, 479 F.2d at 250: "a drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use."

The record discloses that there was no general recognition of Laetrile's effectiveness on October 9, 1962 (Pet. App. 100a-154a, 208a-211a), and the district court indeed upheld the Commissioner's finding to that effect (Pet. App. 22a). Thus, as a drug offered for use in the treatment of a life-threatening disease, Laetrile could not meet the 1962 grandfather clause requirement of achieving general recognition of safety because it had not achieved general recognition of effectiveness. This consideration reinforces the Commissioner's conclusion based on the evidence concerning safety itself.

d. *Labeling.* To show that Laetrile labeling existed in 1962, the district court relied solely on the affidavit of Robert S. K. Young, M.D., Ph.D., which stated that 1962 labeling had characterized Laetrile as a palliative agent for use in " 'cancers beyond aid by standard agents' " and had warned that " 'it is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated' " (Pet. App. 15a n.7; A. 63). What the district court did not note is that Dr. Young's affidavit referred to labeling that was proposed for Laetrile as a drug in investigational use. This was the labeling included in the NDA submitted by Ernst Krebs, Jr., on October 3, 1962 (see Pet. App. 191a-192a). This labeling thus was not for a product commercially sold or used on October 9, 1962. Moreover, Dr. Young stated that, in fact, the 1962 proposed labeling differed significantly from 1965 labeling in FDA's possession (A. 63-66).

The Commissioner's finding that "Laetrile as now known is not intended solely for use under conditions recommended in labeling on October 9, 1962" (Pet. App. 199a) is supported by substantial record evidence (Pet. App. 191a-199a). This included evidence that, in contrast to the labeling suggested by Ernst Krebs, Jr., on October 3, 1962, Laetrile was described after 1962 as a therapy that could, and should, be used to the exclusion of other cancer therapies (Pet. App. 196a-197a). There was also

evidence that oral administration of Laetrile first appeared after 1962 (Pet. App. 194a-195a, 198a, and that suggested dosages have ranged from 1.5 grams to more than 9 grams, with no scientific rationale to account for the differing recommendations (Pet. App. 192a, 196a).[34] The district court's reversal of the Commissioner's finding was erroneous.

3. In sum, the Commissioner, supported by substantial evidence of record, concluded that Laetrile failed to satisfy four separate and necessary conditions for grandfather status under the 1962 amendments. This conclusion is in accord with the decisions of all federal courts that have considered the issue, with the exception of the district court below and a few district courts that have relied on the decisions below in granting preliminary relief.[35] With

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[34] Indeed, the record indicates an absence of any uniform standard or generally recognized labeling either before or after 1962. For example, pre-1962 labeling varied widely with respect to the proper method of administration; suggested methods included injection into muscles and "Iontophoresis," a method—which the Commissioner termed "bizarre" (Pet. App. 193a)—employing galvanic current to force Laetrile into the cancer cells (Pet. App. 193a-194a).

[35] Subsequent to the district court's initial decision (A. 20-30), similar actions were instituted by cancer patients in other courts. In *Carnohan* v. *United States*, No. 77-0010 (S.D. Cal. Jan. 6, 1977), and *Rizzo* v. *United States*, 432 F. Supp. 356 (E.D. N.Y. 1977), the district courts, relying on the initial decision of the court of appeals below (A. 31-41), granted preliminary injunctions allowing plaintiffs to transport Laetrile in interstate commerce. Both cases were dismissed upon the death of the plaintiffs. Three other cases were dismissed after temporary restraining orders were granted. See, *e.g.*, *Keene* v. *United States*, No. 76-0249 (S.D. W.Va., dismissed Sept. 28, 1976).

those exceptions, the federal decisions concerning Laetrile (or related drugs under other names) have held that it is a new drug fully subject to the statutory requirements that safety and effectiveness be shown by scientific evidence, or have concluded on requests for preliminary relief that the likelihood of success on that issue lies with the government. See, *e.g.*, *United States* v. *Mosinee Research Corp.*, 583 F.2d 930, 932 (7th Cir. 1978); *United States* v. *Spectro Foods Corp.*, Civ. No. 76-101 (D. N.J. Jan. 29, 1976), aff'd in pertinent part, 544 F.2d 1175, 1179-1180 (3d Cir. 1976); *Hanson* v. *United States*, 417 F. Supp. 30, 34-36 (D. Minn. 1976), aff'd, 540 F.2d 947 (8th Cir. 1976); *United States* v. *Earthco*, No. CV 78-3602-HP (C.D. Cal. Jan. 24, 1979); *Gadler* v. *United States*, 425 F. Supp. 244, 247-249 (D. Minn. 1977); *In re Morgan* v. *Matthews*, No. 76-1637 (D. S.C. Nov. 30, 1976); *United States* v. *General Research Laboratories*, 397 F. Supp. 197, 199 (C.D. Cal. 1975).

In extending grandfather protection to Laetrile, which was not an established anti-cancer drug generally recognized by experts as safe prior to October 9, 1962, the district court disregarded the teaching of this Court that liberality in the construction of the Act does not justify carving out exemptions, but "more appropriately belongs to enforcement of the central purpose of the Act" (*United States* v. *Dotterweich*, 320 U.S. 277, 284 (1943)). The district court applied an improper standard of review to the Commissioner's factual findings on all four of the points

at issue, and erred in failing to sustain those findings. Thus the district court's holding that Laetrile is exempt under the 1962 grandfather clause provides no basis for affirming the judgment of the court of appeals.

III

NO CONSTITUTIONAL RIGHT OF PRIVACY ENJOYED BY TERMINALLY ILL CANCER PATIENTS OR ANYONE ELSE PROTECTS ACCESS TO A DRUG SUCH AS LAETRILE

The district court held that "[b]y denying the right to use a nontoxic substance [Laetrile] in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a). This holding is erroneous and affords no ground for sustaining the decision of the court of appeals. First, the holding is premised on the court's unwarranted belief, contrary to the well-supported findings of the Commissioner, that Laetrile has been shown to be nontoxic. Second, even if Laetrile were not toxic, there is no constitutional right to take any particular drug or class of drugs for medical purposes. Third, even if the constitutional right of privacy would otherwise include a right to take particular drugs for medical purposes, any such right to use Laetrile is outweighed by a compelling governmental interest in protecting the public health and welfare.

A. In Declaring Laetrile to be Nontoxic the District Court Improperly Contradicted the Well-Supported Findings of the Commissioner

The district court's constitutional holding was premised on its view that Laetrile is "nontoxic" and "innocuous" (Pet. App. 38a, 41a). The court stated that "the vast amount of practical experience of actual experimenters and users, in administering Laetrile both parenterally and orally, has established its nontoxicity" (Pet. App. 29a n.18).[36] In so determining, the court contradicted the findings of the Commissioner. As related above (pages 7-9, *supra*), the Commissioner found that Laetrile has not been adequately tested for safety and that it is not generally recognized by experts as safe for use in man (Pet. App. 154a-162a). These findings were based on a review of the scientific literature (Pet. App. 155a-157a) and on the testimony of experts, who testified that the safety of Laetrile has not been demonstrated and that there are definite indications that, at least in its oral form, Laetrile is toxic (Pet. App. 155a-162a, 254a-257a, 271a). The findings were also based on recognition by Laetrile's pro-

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[36] The court gave two citations for this statement, neither of which supports it. Footnote 15 of the court's opinion (Pet. App. 24a) discusses the placebo effect of Laetrile, not its safety. Page 311 of the transcript reports the testimony of plaintiff Rutherford, a user of Laetrile and not a scientist, that he uses one 500 milligram tablet "to as high as nine of them in a day's time depending on what this carcass is telling me * * *" (A. 85).

ponents of the possible toxicity of the drug in its oral form (Pet. App. 86a-88a, 158a, 254a-255a).[37]

In rejecting the Commissioner's findings, the district court relied on one laboratory study and the views of Laetrile practitioners (Pet. App. 31a n.23). The laboratory study,[38] though not specifically discussed in the Commissioner's opinion, was impugned as a scientific endeavor by a toxicologist who reviewed it,[39] and the Commission obviously rejected it as sound evidence upon which to conclude that Laetrile is not toxic (Pet. App. 155a-162a). The court's reliance on the casual observations of physicians who

[37] As noted earlier (page 9, note 8, *supra*), reports appearing in the medical literature after the administrative hearing support the toxic nature of oral Laetrile and raise new questions about its toxicity in other forms.

[38] The study was conducted by Harold Manner, Ph.D., a professor of biology (R. 262). ("R." refers to the record in the hearing before the Commissioner.) He injected Laetrile at various doses into mice for 15 days. No mice died as a result, although loss of hair and hyperactivity were observed at higher doses. It appears that Dr. Manner assessed toxicity reactions on the basis of visual examinations and weight gain only. He did not perform drug chemical analyses of animal tissues or fluids. See note 39, *infra*.

[39] The record contains the affidavit of Jacqueline Verrett, Ph.D., a toxicologist, who criticized the Manner data as unscientific and unreliable (R-427): "The authors did not report the performance of any clinical chemical tests (especially cyanohemoglobin determinations), nor the necropsing of the mice *or* the performance of microscopic study of the tissues. Therefore, it cannot be determined whether there were changes in the chemical status of the mice * * * in the tissues as a result of the administration of amygdalin." She concluded that the study was "inadequate for determining that amygdalin was safe for human consumption."

advocate Laetrile in their practices was equally inappropriate. See *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 619.[40]

In any event, the court had no warrant to weigh the scientific evidence afresh; it was "hardly qualified to second guess" the scientific judgment of the Commissioner. *United States* v. *An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 792 (1969). It was error for the court to ignore the considered opinions of leading cancer specialists on which the Commissioner relied, and to accept instead the anecdotal experiences of a handful of Laetrile practitioners who themselves are not qualified experts. The Commissioner's finding that Laetrile had not been shown to be safe was supported by the evidence and should have been upheld. See *Citizens to Preserve Overton Park* v. *Volpe*, *supra*, 401 U.S. at 413-414. Thus, the court's constitutional holding, taken on its own

[40] The district court relied on the personal experience of Drs. Binzel, Thompson, McDonald and Nieper. Pet. App. 31a-32a. The qualifications of Drs. Thompson and Nieper are not contained in the record. The Commissioner concluded that Drs. Binzel and McDonald lacked training and experience in oncology or drug evaluation. *Id.* at 150a-151a. The court also relied on two affidavits, apparently executed for another proceeding, in which Drs. Gurchot and Leake stated that Laetrile was used experimentally between 1934 and 1945 and was recognized then as being safe. *Id.* at 31a-32a n. 23. These assertions are in dispute (*id.* at 206a-208a) and, in any event, are not supported by data purporting to show Laetrile's nontoxicity. The composition, purity, and strength of the Laetrile Gurchot and Leake discuss are different from those of the Laetrile in use today. *Id.* at 171a-172a.

terms, must fall because of the erroneous factual assumption on which it is based.

B. The Constitutional Right of Privacy Does Not Include a Right to Use Unproven or Ineffective Drugs

This case arises against the background of a long Anglo-American tradition of government protection of the public from unsafe, worthless, or fraudulent foods and drugs. As the historical survey in the Appendix to this brief notes, the sale of food "not wholesome for man's body" was first prohibited by an English statute passed in 1266 (51 Henry III, c. 6), and the regulation of drugs in England dates from the mid-sixteenth century.[41] The advances of modern science since the mid-nineteenth century have made possible, for the first time in human history, the broad application of scientific principles to the treatment of human disease. These advances have also made possible more precise evaluations of the identity and effects of drugs. They have thereby established the basis for a system of drug regulation in this country that protects the public in a rational and scientifically informed way against unsafe or ineffective drugs.

The constitutional privacy claim asserted by respondents and upheld by the district court in this case thus challenges the foundations of a centuries-old function of government. The challenge takes aim, not at the administrative action of the Commissioner, but at the Federal Food, Drug, and Cosmetic Act

[41] See G. Clark, *A History of the Royal College of Physicians of London* 80, 82-83 (1964); see App., *infra*, 1a-3a.

itself, since the Commissioner has correctly applied the Act in reaching his decision (see Points I and II, *supra*). If the challenge were to succeed, it would disable not only the federal government, but the states as well, from protecting the public against worthless drugs. The challenge, however, must fail, for it has no support in the privacy decisions of this Court.

1. As the Court has observed, "Virtually every governmental action interferes with personal privacy to some degree. The question in each case is whether that interference violates a command of the United States Constitution." *Katz* v. *United States*, 389 U.S. 347, 350 n.5 (1967). We do not dispute that the personal health care of cancer patients who wish to take Laetrile—as well as the financial interests of those who manufacture and distribute the drug—is affected by the application to Laetrile of the safety and effectiveness requirements of the Act and the consequent prohibition of the drug's importation or introduction into interstate commerce until the statutory requirements are met.[42] But the Constitution does not necessarily forbid that result. This Court's decisions recognizing a constitutional right of privacy do not deny Congress the power to protect the public health and welfare by enacting laws to assure that medical drugs available to the public are safe and effective for their intended use, even if such laws

[42] See Sections 301(d) and 304 of the Act, 21 U.S.C. 331(d) and 334; see also 18 U.S.C. 545. No provision of federal law directly prohibits personal use or affects any supply that has neither been imported nor had any connection with interstate commerce.

interfere with an individual's access to an unproven drug that a court believes to be nontoxic. To read the Court's decisions as requiring such a result would be to invoke the right of privacy in place of freedom of contract, see *Lochner* v. *New York*, 198 U.S. 45 (1905), as a basis for substituting the will of the courts for the judgment of Congress concerning how best to protect the public health and welfare. See *Whalen* v. *Roe*, 429 U.S. 589, 596-597 (1977).

This Court's recognition of a constitutional right of privacy has its main roots in the dissenting opinion of Mr. Justice Brandeis in *Olmstead* v. *United States*, 277 U.S. 438, 471-485 (1928), and the decision of the Court in *Griswold* v. *Connecticut*, 381 U.S. 479 (1965). In *Olmstead*, Mr. Justice Brandeis discerned in the Constitution an intent to "protect Americans in their beliefs, their thoughts, their emotions and their sensations" and in "the right to be let alone—the most comprehensive of rights and the right most valued by civilized men." 277 U.S. at 478. In *Griswold*, this Court identified a "zone of privacy created by several fundamental constitutional guarantees" (381 U.S. at 485), and held that a state law making it a crime for any person to use any drug or article to prevent conception violated a right of marital privacy that falls within that zone.

The dimensions of the constitutional right of privacy have gradually emerged since *Griswold*. In *Whalen* v. *Roe*, 429 U.S. 589, 599 (1977), the Court described its "privacy" cases as involving "at least two different kinds of interests." One it defined as

"the individual interest in avoiding disclosure of personal matters," and the other as "the interest in independence in making certain kinds of important decisions." *Id.* at 599-600. To these may be added an interest in freedom from unwarranted intrusions into the human body. See *Schmerber* v. *California*, 384 U.S. 757, 766-767 (1966).

Nothing suggests that the nondisclosure interest is involved in this case. Neither can it be said that intrusions into the human body are involved, for the federal laws at issue here do not require cancer patients to undergo particular forms of treatment, or any treatment at all.[43]

In holding that the Constitution guarantees a right to use substances not proven toxic "in connection with one's own personal health-care" (Pet. App. 41a), the district court relied primarily on cases involving

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[43] The Court has upheld physical intrusions in *Jacobson* v. *Massachusetts*, 197 U.S. 11 (1905) (compulsory smallpox vaccination); *Buck* v. *Bell*, 274 U.S. 200 (1927) (compulsory sterilization of certain persons adjudged mentally defective); and *Schmerber* v. *California*, *supra*, 384 U.S. 757 (compulsory drawing of blood sample for analysis of alcohol content). And the Court has relied on *Jacobson* and *Buck* to reject the suggestion that "an unlimited right to do with one's body as one pleases bears a close relationship to the right of privacy previously articulated in the Court's decisions." *Roe* v. *Wade*, 410 U.S. 113, 154 (1973). Those cases can also be viewed, however, as involving intrusions into a constitutionally protected zone of privacy that were warranted by what were judged to be compelling state interests, expressed through laws reasonably related to those interests. See page 68, *infra*.

the privacy interest in "independence in making certain kinds of important decisions"—particularly the cases of *Doe* v. *Bolton*, 410 U.S. 179 (1973), and *Roe* v. *Wade*, 410 U.S. 113 (1973), both concerned with abortion.[44] But this Court's view of that line of cases makes it clear that they do not support the claim made here. The Court has characterized those cases as dealing with "matters relating to marriage, procreation, contraception, family relationships, and child rearing and education." *Paul* v. *Davis*, 424 U.S. 693, 713 (1976); see *Whalen* v. *Roe*, *supra*, 429 U.S. at 600 n.26 (quoting same statement). The right claimed here of caring for one's health by obtaining a particular drug without government hindrance does not fall into any of those categories. Without belittling the desperate predicament of a person threatened with death from cancer or other disease, and without denying that life may be at stake in any medical decision made by or for that person, the fact remains that the decision to take a particular drug in an effort to prolong life or cure disease is a technical, instrumental decision—a decision as to how best to achieve a hoped-for medical effect. It is not among the "certain kinds of important decisions" to which the Court

[44] Other cases in this category include *Loving* v. *Virginia*, 388 U.S. 1 (1967) (choice of spouse); *Griswold* v. *Connecticut*, *supra* (decision to use contraceptives); *Pierce* v. *Society of Sisters*, 268 U.S. 510 (1925) (choice of children's school); *Meyer* v. *Nebraska*, 262 U.S. 390 (1923) (choice of a legitimate vocation).

referred in *Whalen* v. *Roe*, *supra* (429 U.S. at 599-600).[45]

2. This Court has recognized that decisions of the kind at issue here, involving the efficacy or safety of drugs or medical treatments, are not among the kinds of decisions protected by the constitutional right of privacy.[46] In a series of abortion and contraception

[45] Nor does the claimed constitutional right of free choice with respect to medical drugs implicate the First Amendment values that have informed decisions such as *Stanley* v. *Georgia*, 394 U.S. 557, 565 (1969) (holding that a state may not prohibit possession of obscene materials in one's home). Cf., *e.g.*, *United States* v. *12 200-Ft. Reels of Film*, 413 U.S. 123, 128 (1973) (importation of obscene matter may be prohibited even when for private use only; "[t]o allow such a claim would be not unlike compelling the Government to permit importation of prohibited or controlled drugs for private consumption as long as such drugs are not for public distribution or sale").

[46] The authority of government, in some circumstances, to override individual choice in matters not affecting others was reaffirmed in *Paris Adult Theater I* v. *Slaton*, 413 U.S. 49 (1973). The Court stated: "[F]or us to say that our Constitution incorporates the proposition that conduct involving consenting adults only is always beyond state regulation is a step we are unable to take" (*id.* at 68), and explained (*id.* at 68 n.15):

> The state statute books are replete with constitutionally unchallenged laws against prostitution, suicide, voluntary self-mutiliation, brutalizing "bare fist" prize fights, and duels, although these crimes may only directly involve "consenting adults". Statutes making bigamy a crime surely cut into an individual's freedom to associate, but few today seriously claim such statutes violate the First Amendment or any other constitutional provision. [Citations omitted.]

cases the Court has emphasized that, although the laws in question were unconstitutional because they impinged on the right of independent decision-making with respect to pregnancy and procreation, government restrictions on that right are justified when they serve compelling interests in "safeguarding health, [or] in maintaining medical standards * * *." *Roe* v. *Wade*, *supra*, 410 U.S. at 154; see also *id.* at 162-164; *Doe* v. *Bolton*, *supra*, 410 U.S. at 189; *Planned Parenthood of Missouri* v. *Danforth*, 428 U.S. 52 (1976); *Carey* v. *Population Services International*, 431 U.S. 678, 685-686 (1977). Indeed, in *Roe* v. *Wade* the Court observed that "[t]he State has a legitimate interest in seeing to it that abortion, like any other medical procedure, is performed under circumstances that insure *maximum* safety for the patient" (410 U.S. at 150; emphasis added), and the Court listed a number of the measures that a state may permissibly take to regulate abortion in furtherance of its interests "in the areas of health and medical standards" (*id.* at 149).[47] Thus, the abortion

[47] The government may require that abortions be performed (after the first trimester) only at licensed institutions that "insure maximum safety for the patient" and may prohibit any abortion performed by a person not a physician (*id.* at 150, 165). The state may also totally prohibit an abortion during the third trimester of pregnancy (*id.* at 165); its interest in doing so is constitutionally justified even apart from its interest in protecting prenatal life, since "the State retains a definite interest in protecting the woman's own health and safety when an abortion is proposed at a late stage of pregnancy" (*id.* at 150). Of course, the state may impose these restrictions on a woman's abortion right even when the woman is fully aware of the risks and willing to take them.

laws at issue in *Roe* v. *Wade*, *Doe* v. *Bolton*, and *Planned Parenthood* v. *Danforth* were struck down not because they interfered in health care decisions, but because they demonstrably were not designed to serve any health interest.

This point was made most clearly in *Planned Parenthood* v. *Danforth*, where the Court struck down a state prohibition of a particular abortion procedure, saline amniocentesis. Quoting *Roe* v. *Wade*, the Court defined the issue before it as "[w]hether the flat prohibition of saline amniocentesis is a restriction which 'reasonably relates to the preservation and protection of maternal health.'" 428 U.S. at 76. The Court cited voluminous record evidence of the safety and effectiveness of saline amniocentesis, in comparison with other available abortion procedures, and concluded that the state prohibition bore no reasonable relationship to protection of maternal health. 428 U.S. at 78-79.

The Court's recognition of the government's interest in protecting the health of its citizens was reiterated in *Carey* v. *Population Services International*, *supra*, 431 U.S. at 678. There, while disclaiming any view that "there is an independent fundamental 'right of access to contraceptives'" (*id.* at 688), the Court struck down a law restricting access to that particular category of drugs and medical devices[48]

[48] "Barrier" contraceptives are medical devices regulated under the Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 579 (1976). Birth control pills are drugs regulated under the drug provisions of the Food, Drug, and Cosmetic Act.

"because such access is essential to exercise of the constitutionally protected right of decision in matters of child-bearing" (*ibid.*) (citing *Roe* v. *Wade*, *supra*, and *Griswold* v. *Connecticut*, *supra*). Still, the Court did not hold that there is a constitutional right of access to all contraceptives, regardless of their safety and efficacy. The Court cited the Federal Food, Drug, and Cosmetic Act—including the drug regulation provisions at issue in this case—as among federal and state laws "that comprehensively regulate hazardous drugs and devices" (431 U.S. at 690 n.9), and suggested that in light of those laws the state anti-contraceptive statute at issue in *Carey* did not serve any "health-related interest" (*ibid.*).[49] The Court also pointed out that the statute was not "designed to serve as a quality control device" (*id.* at 691).

Thus, *Carey*, *Planned Parenthood*, and the other cases invalidating laws restricting the individual's decision with respect to pregnancy and procreation have all distinguished, and preserved, the government's interest in regulation designed to protect the public's health.[50] In this case, we deal with the statute that

[49] In *Eisenstadt* v. *Baird*, 405 U.S. 438 (1972), where the Court struck down under the Equal Protection Clause a state statute prohibiting the distribution of contraceptives to unmarried persons, it similarly referred to "the federal and state laws *already* regulating the distribution of harmful drugs," including the Federal Food, Drug, and Cosmetic Act (*id.* at 452; emphasis in original), as part of its analysis of why the state law at issue did not serve a health purpose.

[50] For a vindication of that interest, see *Fitzgerald* v. *Porter Memorial Hospital*, 523 F.2d 716, 721 (7th Cir. 1975) (Stevens, J.), cert. denied, 425 U.S. 916 (1976), holding that

provides the public's primary protection against unsafe, ineffective, or fraudulent drugs. This statute is specifically designed to serve "as a quality control device." Its clear and direct relationship to health protection is undeniable. At the same time, this case involves no claim bound up with the constitutionally protected right of independent decision-making concerning marriage, pregnancy, and procreation. The Court's privacy decisions hence do not support, but reject, the claim made here of a constitutional right to use a particular medical drug.[51]

"the so-called right of marital privacy does not include the right of either spouse to have the husband present in the delivery room of a public hospital which, for medical reasons, has adopted a rule requiring his exclusion."

[51] In his concurring opinion in *Doe* v. *Bolton*, Mr. Justice Douglas characterized "the freedom to care for one's health and person" as "fundamental" and, therefore, "subject to regulation [only] on a showing of 'compelling state interest.'" 410 U.S. at 213. The district court discerned in this language a right of privacy protecting the acquisition and use of Laetrile (Pet. App. 36a). Mr. Justice Douglas did not go so far, for he recognized the "legitimate objective of preserving the mother's health [that] clearly supports [some abortion] laws." 410 U.S. at 216. Because the Georgia statute "outlaw[ed] virtually all such operations," he concluded that it could not be "seriously urged that so comprehensive a ban is aimed at protecting the woman's health." 410 U.S. at 216-217. The Federal Food, Drug, and Cosmetic Act, by contrast, does not comprehensively ban all drugs for cancer treatment, but only those not shown to be safe and effective. In any event, Mr. Justice Douglas's conception of health care as a separate privacy right under the Constitution has not won the support of the Court.

3. This conclusion is confirmed by a statement the Court made in *Whalen* v. *Roe*, 429 U.S. 589 (1977). The question there was whether a state may record in a centralized computer file the names and addresses of persons who obtain certain prescription drugs for which there is a lawful and an unlawful market; the Court held that it may, without violating any constitutional right to privacy. In discussing the privacy claim, the Court commented: "the State no doubt could prohibit entirely the use of particular Schedule II drugs * * *" (*id.* at 603).[52] Schedule II drugs "have accepted uses in the amelioration of pain and in the treatment of [various diseases]" (*id.* at 593 n.8); they are safe and effective, but are also liable to abuse. If a state may prohibit entirely the use of such drugs—which can provide important therapeutic benefits to some patients—then *a fortiori* the government in this case may prohibit interstate commerce in a drug that has no recognized medical use in the treatment of the life-threatening disease for which it is recommended, and which has a potential for harming, at the least, those patients who are deterred by the drug's availability from seeking effective treatment.

[52] In a footnote at this point (*id.* at 603 n.30) the Court stated: "It is, of course, well settled that the State has broad police powers in regulating the administration of drugs by the health professions," citing *Robinson* v. *California*, 370 U.S. 660, 664-665 (1962); *Minnesota ex rel. Whipple* v. *Martinson*, 256 U.S. 41, 45 (1921); and *Barsky* v. *Board of Regents*, 347 U.S. 442, 449 (1954).

The dictum in *Whalen* v. *Roe* thus underscores the lesson of the Court's privacy decisions. As the abortion and contraception cases expressly recognize, the government has an interest in the health of its citizens which justifies health-related restrictions on established constitutional privacy rights. If that is so, then surely freedom from government health regulation of drugs is not itself a constitutionally protected right.

4. The contours of this case are deceivingly narrow. The constitutional claim may be urged in this Court only in support of a judgment that prohibits the government from interfering with access by "terminally ill" cancer patients to supplies of Laetrile intended for intravenous administration under the direction of a physician.[53] But the logic of the claim goes much further. If, as the district court held, there is a constitutional right of access to any drug not *proven* toxic, then it is difficult to see how the safety and efficacy requirements of the Act can be constitutionally enforced with respect to *any* drug if a court decides the drug is nontoxic, a physician somewhere is willing to prescribe it, and an individual wishes to take it. Already, a group of patients suffering from adrenal corticol insufficiency, a condition treatable by the use of steroid compounds approved under Section 505 of the Act, have brought suit in the same district court that decided this case to prohibit the FDA from enforcing the requirements of the Act with respect to a new drug described as

[53] See page 2, note 1, *supra*.

adrenal corticol extract.[54] Other patients claiming a constitutional right to receive marijuana for medical purposes have filed district court suits to vindicate that right.[55] And the constitutional claim would be equally fatal, of course, to state as to federal regulation. We submit that this Court's privacy decisions require no such results.

C. Application to Laetrile of the Safety and Efficacy Requirements of the Food, Drug, and Cosmetic Act Is a Reasonable Means of Serving a Compelling Government Interest in Protecting the Public Health

Even "fundamental" rights are not absolute; they may constitutionally be restricted if the restrictions are justified by a "compelling" governmental interest. *Roe* v. *Wade*, *supra*, 410 U.S. at 155; *Carey* v. *Population Services International*, *supra*, 431 U.S. at 686. If this Court were to recognize, contrary to our submission, a constitutional right of access to unproven drugs "in connection with one's own personal healthcare," enjoyed either by terminally ill patients or by members of the public generally, it should nonetheless reject the constitutional claim in this case. It should do so on the ground that application of the Food, Drug, and Cosmetic Act to Laetrile is justified by compelling governmental interests in protecting the public health, reinforced by a legitimate interest in preventing fraud.

[54] *American Academy of Medical Preventics* v. *Califanó*, No. 79-60-E (W.D. Okla., filed Jan. 16, 1979).

[55] See, *e.g.*, *Mayerson* v. *Bensinger, et al.*, No. 78-2707 (E.D. Pa., filed Aug. 11, 1978); *Hartz* v. *Bensinger, et al.*, 461 F. Supp. 431 (E.D. Pa. 1978).

1. There is a compelling governmental interest in maintaining a system for the scientific evaluation of the safety and effectiveness of drugs before they are permitted to be marketed. Laymen generally are not qualified to determine whether a particular course of therapy will be effective. Even individual physicians are not in a position to determine scientifically which drugs on the market are effective. *Upjohn Co.* v. *Finch*, 422 F.2d 944, 952-954 (6th Cir. 1970). As a consequence, Congress decided that an expert scientific agency should make that determination—on the basis of information submitted by the manufacturer or promoter—before the drug is permitted to be marketed.

When Congress amended the Food, Drug, and Cosmetic Act in 1962, the House Report noted:

> [M]any new drugs that have cleared the safety requirements of the law are marketed with unproved claims of therapeutic effectiveness. As a result, good medical practice is hampered, and the consumer is misled until, perhaps years later, the Government has gathered the necessary evidence to sustain its burden of proving the violation in court.

H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). The effect of invalidating the statute or judicially exempting Laetrile would be to deprive the public of assurance that drugs on the market have "the reliability and effectiveness" Congress intended. S.

Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 17 (1962).[56]

Having reasonably concluded that unsafe or ineffective drugs are harmful to the public health, Congress established a system requiring the Commissioner to determine that a new drug is safe and effective before it may be marketed in interstate commerce. In this case, acting within the authority granted him by the statute, the Commissioner has determined that Laetrile has not met the requirements imposed by the Act. That the factual issues may be in dispute does not disable the government from acting, for this Court long ago established that a legislature is "not compelled to commit a matter involving the public

[56] The history of cancer therapy in this country confirms the justification for legislative concern that, without premarketing clearance, useless drugs would flourish to the detriment of the public health. As the Commissioner found, there has been a long and sorry history of cancer quackery, during which "literally thousands of supposed remedies for cancer" have been promoted. Pet. App. 212a-217a. For example, in the 1940's and early 1950's cancer patients paid as much as $300 per injection for the worthless Koch's Synthetic Antitoxins. *Id.* at 214a. Harry Hoxsey promoted his unproven cancer remedy for more than 30 years in spite of numerous local, state, and federal court actions, until a permanent injunction was finally issued in 1960, at which time more than 10,000 patients were receiving the remedy. *Id.* at 214a-215a. Krebiozen was another remedy popular in the 1960's. *Id.* at 215a-217a. (The proponents of Krebiozen also brought a suit to force the FDA to allow the marketing of an unapproved new drug. See *Rutherford* v. *American Medical Association*, 379 F.2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043 (1968).)

health to the final decision of a court or jury." *Jacobson* v. *Massachusetts*, *supra*, 197 U.S. at 30.[57] Congress has sought to preserve public and professional confidence in the safety and efficacy of the drug supply by committing such decisions to the Commissioner. This interest is a compelling one, and the resulting restriction on the interstate distribution of Laetrile is reasonably and indispensably related to it.

2. The government also has a compelling interest in preventing the marketing of ineffective drugs in order to promote the timely treatment of illness with safe and effective drugs. As Senator Kefauver pointed out when introducing the 1962 amendments: "An otherwise completely safe drug can be dangerous to the patient if it does not have the therapeutic effect in use which it is represented to have." 107 Cong. Rec. 5640 (1961).[58] This fact is poignant because a

[57] See also *Fitzgerald* v. *Porter Memorial Hospital*, *supra*, 523 F.2d at 721:

> [T]he dispute within the medical profession as to the propriety and safety of permitting the husband to be present during the routine birth is not one that should be resolved by substituting our judgment for the professional judgment of the staff of defendant hospital. [Footnote omitted.]

[58] The legislative concern that credulous and desperate laymen will rely on the claims made for ineffective drugs and thus delay treatment by recognized therapy, or that even physicians will believe false claims and prescribe ineffective drugs in place of more reliable substitutes, is well justified See, *e.g.*, *Durovic* v. *Richardson*, *supra*, 479 F.2d at 251; *Upjohn Co.* v. *Finch*, 422 F.2d 944, 953 (6th Cir. 1970);

significant number of cancer patients can be cured, or enabled to live longer, by legitimate therapy. Pet. App. 227a, 268a; see page 73, note 61, *infra*. The availability of Laetrile encourages delay in obtaining legitimate therapy, or avoidance of such therapy altogether. Pet. App. 228a-242a. And even after patients begin treatment with effective therapy, the readily acknowledged side effects and hazards of that therapy may cause them to abandon it when it might still be beneficial, and turn instead to Laetrile. *Ibid.* The drug's promoters, playing on the patients' fears, actively encourage this process (*id.* at 230a-233a).[59]

The district court was concerned about the "terminally ill" cancer patient. But the record reflects that the prospective identification of a patient as "terminal" is frequently inaccurate, since "[m]any patients who are critically ill respond to modern day management of cancer." Pet. App. 268a. Moreover, there is no proof that Laetrile will not "interfere with

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United States v. *Nutrition Service, Inc.*, 227 F. Supp. 375, 388 (W.D. Pa. 1964), aff'd per curiam, 347 F.2d 233 (3d Cir. 1965).

[59] The district court suggested that constitutional protection may attach to the use of Laetrile because it has a "placebo" effect. Pet. App. 24a, 38a. The placebo effect can occur when an authority figure (usually a physician) administers a drug to the patient with a statement that the drug will prevent cancer, relieve his pain or help him get well. But the placebo effect operates precisely and solely because the patient is deceived into believing that he is receiving a therapeutically effective drug.

the metabolism of and compromise the effects from known anticancer treatments" (*id.* at 271a).[60]

In addition, government acquiescence in the use of Laetrile in the injectable form by the terminally ill may suggest to other cancer patients, including ones in the early stages of the disease and quite susceptible to conventional treatment, that the government accepts the drug as being of some value. They may consequently attempt to secure it, quite possibly in the potentially toxic tablet form, either at Mexican clinics or through illicit channels, to the neglect of their conventional therapy and the detriment of their health. See Pet. App. 268a-271a.[61]

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[60] "Some have suggested that, if legalized, Laetrile should be used only on hopelessly ill patients with cancer. These patients, however, present special problems which have not been adequately investigated. For instance, the acute toxicity of Laetrile in tumor-bearing animals is much greater than is the acute toxicity of Laetrile in non-tumor-bearing animals. This suggests that the more tumor that is present, the more toxic the Laetrile becomes * * *. In addition, these patients invariably have liver and renal damage * * * Laetrile is detoxified by rhodenase which is found in high levels in the liver. Is this same high level found in a cancerous liver? We have no data on this. * * * What is the effect of kidney failure on Laetrile's toxicity? Again, the data are not available." Lewis, *Laetrile*, 127 West. J. Med. 55, 59-60 (1977).

[61] " [*R*]*ecent Trends in Survival of Cancer Patients*, [*1960-1971*] shows that substantial progress has been made in all 17 tumor types indexed. The percent increase in five-year survival rates ranges from 0 for one disease only * * * to 700 percent for acute lymphocytic leukemia in females. The average increase in five year survival for all patients was 75 percent." Lewis, *supra*, 127 West. J. Med. 55. The present survival rate is likely to be higher, but is not known since "the major ad-

Despite the limitation of the court of appeals' judgment to injectable Laetrile provided for the terminally ill, some leakage of drug shipments to persons not within that class may be expected. Indeed, there is evidence that this has occurred in the distribution of Laetrile under the system established by the district court. The affidavit of Gerald M. Rachanow, Consumer Safety Officer in the FDA's Bureau of Drugs (A. 81-84), states that in some instances supplies of Laetrile ordered by patients in the certified class, through physicians designated as purchasing agents, have not been delivered to those patients (A. 82, 83). In other instances, orders have been placed for supplies of Laetrile which the designated patients do not wish to receive (*ibid.*). These practices create supplies of Laetrile available for sale to patients not in the certified class (A. 83-84).[62]

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vances in the past decade in chemotherapy are yet to be adequately recorded by this survey." *Id.* at 56. In view of present progress, abstinence from effective therapy in favor of Laetrile is all the more damaging to the public health.

[62] The course of cancer in the human body is irregular and unpredictable. It is often marked by spontaneous remissions, which may last for extended periods of time (Pet. App. 240a-241a). When a spontaneous remission occurs while a patient is taking a particular drug, it is easy to say that the drug caused the remission; one of the great difficulties in cancer research is distinguishing between spontaneous remissions and those due to a particular drug the patient is taking. If the use of Laetrile or other unproven drugs by cancer patients were permitted, spontaneous remissions occurring during such treatment would induce additional cancer patients to forsake approved (but more painful and inconvenient) treatments in the vain hope that the unproved, and in fact ineffective, drug will provide a cure.

3. Even apart from public health considerations, the government has a strong interest in preventing promoters of useless drugs from deceiving the public.[63] An ineffective drug is a fraud, which wastes the financial resources of the patient and his family. Accordingly, this Court has stated that Congress "surely has great leeway in setting standards for releasing on the public, drugs which may well be miracles or, on the other hand, merely easy money-making schemes through use of fraudulent articles labeled in mysterious scientific dress." *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 622. The social and economic costs that ineffective cancer treatments impose on society are costs Congress sought to prevent when it enacted the statute at issue here.

4. Finally, constitutional protection for Laetrile would inevitably mean constitutional protection for other unproven drugs, both for cancer and for other diseases. Cancer, of course, is not the only disease that may be fatal, and cancer patients not the only ones who may be "terminally ill." Upholding of the district court's constitutional ruling could be expected to produce a heyday for unproven cures, beneficial only to those who sell them. The government's interest in preventing this result, and preserving the public protection now afforded by the Act, is compelling.

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[63] Although commercial speech enjoys First Amendment protection, the state may impose limitations designed to prohibit misleading or deceptive commercial advertising. See *Virginia State Board of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976).

CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

WADE H. MCCREE, JR.
Solicitor General

JOHN H. SHENEFIELD
Assistant Attorney General

STEPHEN R. BARNETT
Deputy Solicitor General

ELINOR HADLEY STILLMAN
Assistant to the Solicitor General

BARRY GROSSMAN
PETER L. DE LA CRUZ
Attorneys

RICHARD M. COOPER
Chief Counsel

EUGENE M. PFEIFER
Associate Chief Counsel for Enforcement
Food and Drug Administration
Department of Health, Education and Welfare

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APPENDIX

GOVERNMENT REGULATION OF DRUGS: AN HISTORICAL SUMMARY

Laws protecting the public from unsafe and fraudulent foods and drugs have a long history in Anglo-American jurisprudence. The sale of food "not wholesome for man's body" was prohibited by an English statute passed in 1266.[1] A 1511 statute provided for punishment of persons who "by crafty means" adulterated edible oils "to the great loss, jeopardy, danger and deceit of [the King's] subjects * * *."[2] The sale of unwholesome food was a misdemeanor at common law.[3]

This English tradition was carried over to the colonies, which enacted laws regulating foods as early as 1646.[4] Regulation of foods on the state level continued until enactment of the federal Pure Food and Drugs Act of 1906. Pub. L. No. 59-384, 34 Stat. 768 (1906).[5]

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[1] 51 Henry III, c. 6 (1266), 1 Pickering, *Statutes at Large* 49-50 (1762) (hereinafter cited as Pickering). See generally Hutt, *The Basis and Purpose of Government Regulation of Adulteration and Misbranding of Food*, 33 FDC L.J. 505 (1978); Hart, *A History of the Adulteration of Food Before 1906*, 7 FDC L.J. 5 (1952).

[2] 3 Henry VIII, c. 14 (1511), 4 Pickering 118-119.

[3] Hutt, *Criminal Prosecution for Adulteration and Misbranding of Food at Common Law*, 15 FDC L.J. 382, 383-390 (1960).

[4] See Hutt, *supra* note 1, at 507-508, n.19.

[5] See Hutt, *supra* note 1, at 509.

Efforts to protect the public health through regulation of medicines and of those who sold and administered them roughly paralleled our forebearers' increasing regulation of the safety and suitability of the food supply. However, for practical and superstitious reasons, public protection against unfit remedies was more difficult to achieve than protection against unwholesome foods.

Until the mid-nineteenth century the history of medicine was in large part the history of ineffective, and quite often toxic, remedies. Before the advent of modern chemistry in the 1850's, the composition of drugs could be concealed with little difficulty.[6] Scientific assessment of safety came later, and of effectiveness, later still. The impetus and methodology for scientific evaluation of drug effectiveness were not developed until the early part of this century and did not achieve acceptance until around the time of the second world war.[7]

Healing has always had mystical and religious overtones. Before the development of modern science,

[6] J. Young, *The Toadstool Millionaires* 209-210 (1961) [hereinafter cited as Young].

[7] See Irons, *The Clinical Evaluation of Drugs*, 93 JAMA 1523-1524 (1929); Leake, *The Pharmacologic Evaluation of New Drugs*, 93 JAMA 1632-1634 (1929); Atkins, *Conduct of a Controlled Clinical Trial*, Brit. Med. J. No. 5510 at 377-379 (1966); Van Winkle, et al., *Laboratory and Clinical Appraisal of New Drugs*, 126 JAMA 958-961 (1944); H. Gold, "Experience in Human Pharmacology," in *Quantitative Methods in Human Pharmacology and Therapeutics* (1959); Gaddum, *Clinical Pharmacology*, 47 Proc. Royal Soc. Med. 195-204 (1954); B. Barber, *Drugs and Society* 19 (1967).

man "naturally ascribe[d] his diseases either to the wrath of a good being or the malice of an evil being."[8] Thus, until roughly the sixteenth century, magicians, priests and kings were regarded as specially qualified for the healing of the sick.[9] The first tentative official efforts at regulation of those practicing medicine date from the passage of the Licensure Act of 1511, which prohibited unlicensed physicians from practicing medicine.[10] In 1518 the College of Physicians, by a Royal Charter from Henry VIII, was given authority to examine physicians' prescriptions for internal and external medicines and to punish "delinquencies" in the medicinal uses "by fines, amercement, imprisoment or other * * * fitting ways."[11] Parliament ratified the Royal Charter in 1523, and, by an Act of Common Council in 1525, required pharmacists to accept prescriptions only from duly qualified and registered practitioners and to keep those prescriptions on file so that members of the College could determine whether the compounds were suitable for medicinal use.[12] By Act of Parliament in 1540, members of the College called "censors" were

[8] E. Maple, *Magic, Medicine and Quackery* 14 (1968) [hereinafter cited as Maple].

[9] Maple, *supra* note 8, at 13-62.

[10] 3 Henry VIII, c. 2, G. Clark, *A History of the Royal College of Physicians of London*, Volume I, 54-55 (1964) [hereinafter cited as Clark].

[11] Clark, *supra* note 10, at 58, 60. Henry VIII was a dedicated apothecary himself and is reported to have devised 230 medical prescriptions. Maple, *supra* note 8, at 75.

[12] Clark, *supra* note 10, at 79.

given additional authority to enter apothecary shops and to condemn unfit medicines.[13]

This effort at comprehensive drug regulation was short-lived. In reaction to the refusal of physicians to treat the poor, Parliament passed in 1542 another statute commonly referred to as the "Quacks' Charter." The Charter castigated the medical profession as "minding only their own lucres" and as having "troubled and vexed * * * honest men and women whom God hath endowed with the knowledge of the nature, kind and operacion of certain herbs, rootes and waters." The Charter granted to folk-healers the authority to cure all maladies apparent on the surface of the body by means of plasters, poultices, and ointments.[14] Quackery thus became the officially sanctioned medicine for the poor. However, in 1553 the authority of the College of Physicians to enter apothecary shops and inspect drug prescriptions and medicines was reinstituted by Parliament, in an Act which additionally made refusal to permit inspection subject to a fine of ten pounds.[15]

Enforcement efforts still were not undertaken on a comprehensive scale; they consisted mainly of fines and condemnation proceedings against patently defective medical merchandise[16] and of imprisonment

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[13] *Id.* at 82-83, 92.

[14] *Id.* at 86. See also Maple, *supra* note 8, at 65.

[15] Clark, *supra* note 10, at 88.

[16] Maple, *supra* note 8, at 95 (condemnation in 1671 of an entire stock of defective spectacles).

of "imposters."[17] In 1748, the Apothecaries' Act was passed to protect the public against unqualified pill-makers.[18] Nevertheless, England remained the province of those peddling unproven remedies such as "Payne's Medicine for the cure of forgetfulness."[19]

The situation was similar in the American colonies. "[T]he emigrant who sought refuge in the New World would find that the medical quack had arrived before him * * *."[20]

American attempts to curtail fraudulent cures date at least to 1630, when a Massachusets colonist was fined (or whipped) for vending a cure for scurvy determined to be "a water of no worth nor value."[21] In 1649, Massachusetts passed "An Act Respecting Chirurgions, Midwives and Physicians," prohibiting them from "any act contrary to the known approved Rules of Art * * *"; New York passed a similar act in 1684.[22] In 1699 Massachusetts passed a quar-

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[17] Wright and Dobbs, *Quacks Through The Ages*, 105 J. Roy. Soc. Arts. 161, 162-163 (1957).

[18] Maple, *supra* note 8, at 113.

[19] Maple, *supra* note 8, at 126. Following the earthquake of 1755 in Lisbon, one English vendor is reported to have offered pills "good for the earthquake." *Id.*

[20] Maple, *supra* note 8, at 157.

[21] Young, *supra* note 6, at 16-17.

[22] General Laws and Liberties of the Massachusetts Colony, page 28 (1672); 1 Colonial Laws of New York, ch. 5, page 146 (1894). These Acts may be found in the American-British Law Division, Library of Congress, by courtesy of James W. Elder, Librarian.

antine regulation to control smallpox epidemics.[23] Virginia passed an act in 1736 to regulate "the true value of the medicines administered by any practicer in phisic," which required that the composition of "any pills, bolus, portion * * * or any medicines" be expressed in "every particular" upon the practitioner's bill.[24] In 1773 the Connecticut colonial assembly outlawed the activities of mountebanks for a variety of social ills and the sale of "unwholesome and oftentimes dangerous drugs."[25] Continental Army commanders ordered the innoculation of troops in Boston shortly before the Declaration of Independence, in 1776, and General Washington ordered mass innoculation on January 6, 1777.[26]

Legislation to control the quality of drugs began in earnest with an 1808 Louisiana statute proscribing drug adulteration; by 1865 at least 14 states had passed legislation to control the quality of drugs.[27] The Code of Tennessee referred to adulteration that would "lessen the efficacy or change the operation [of

[23] J. Blake, *Public Health in the Town of Boston, 1630-1822* 32-36 (1959).

[24] 4 Henings, *Statutes at Large* 509-510 (1814).

[25] Young, *supra* note 6, at 191.

[26] S. Bayne-Jones, *The Evolution of Preventive Medicine in the United States Army, 1607-1939* 51-52 (1968). See also F. Packard, *History of Medicine in the United States*, 83-84, 578 (1963).

[27] J. Blake, *Safeguarding the Public, Historical Aspects of Medical Drug Control* 100-101 (1970) [hereinafter cited as Blake].

drugs in a manner] injurious to health."[28] The first federal law was the Import Drugs Act of 1848, ch. 70, 9 Stat. 237.[29] It was reported that in the first ten months following enactment of this statute, 90,000 pounds of drugs were refused admission to the country after examination of their quality, purity, and fitness for medical purposes.[30]

By 1879, at least 25 states and territories had enacted statutes to control drug adulteration.[31] A steady growth in state regulation of adulterated drugs continued, and by 1900, 45 states and territories had adopted legislation that typically prohibited adulteration of a drug "with the effect of weakening or destroying its medicinal power."[32]

The first general federal statute regulating the quality of drugs was the Pure Food and Drugs Act of 1906, passed on June 30 of that year. 34 Stat. 768. The Act prohibited the misbranding and adulteration of drugs. The first major challenge to the Act involved a number of drugs, including "Cancerine tablets," that were offered as "Dr. Johnson's Mild Combination Treatment for Cancer, Tumor and Other Chronic Diseases." *United States* v. *Johnson*, 177 Fed. 313 (W.D. Mo. 1910). The district court dismissed an

[28] *Id.* at 101, n.17.

[29] *Ibid.*

[30] *Adulteration of Drugs*, 15 Am. J. Pharm. 382-383 (1849), cited in Blake, *supra*, note 27, at 102, n.19.

[31] Blake, *supra* note 27, at 106.

[32] Blake, *supra* note 27, at 106-107.

indictment alleging that Dr. Johnson had misbranded the drugs because they were not effective in the treatment of cancer. This Court affirmed on the ground that Congress had only sought to prohibit misleading statements made with respect to a drug's ingredients, not with respect to its effectiveness. *United States* v. *Johnson*, 221 U.S. 488 (1911). Congress reacted the next year, 1912, by passing the "Sherley Amendment," 37 Stat. 416, which defined the term "misbranded" so as to include any statement "regarding the curative or therapeutic effect of such article * * * which is false and fraudulent."

Twentieth-century history of federal regulation of drugs is in large measure the history of a contest between the promotion of unproven remedies for common, serious diseases and the law's demand that therapeutic claims be proved. Beginning in 1908 the FDA's annual reports reflect a continuing concern about remedies promoted fraudulently as "a panacea" for diseases, and about supposed remedies that lead purchasers to "lose valuable time which could be employed to advantage by resorting to" proper treatment.[33]

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[33] See P. Dunbar, *Federal Food, Drug, and Cosmetic Law Administrative Reports 1907-1949* 58 (1951) [hereinafter cited as Dunbar]. In 1911 the FDA again noted that reliance on "so-called 'cancer cures' * * * may cause the loss of invaluable time" in the treatment of the condition. *Id.* at 224-225 (characterizing false cancer remedies as "a definite public health menace"). The 1930 FDA Report stated that such remedies may not only harm the user but "cause delay in resorting to rational methods of treatment." *Id.* at 723. This

Cancer is among the diseases most frequently claimed as being curable in a simple, painless way by a new or rediscovered method of treatment.[34] These asserted cures have included "Radol," claimed to be radioactive water, but actually ordinary water;[35] cloth bags consisting of sand and boneblack, which absorb "cancer poison;"[36] a paste made from lim-

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concern was reiterated in the annual reports for 1931, 1942-1943, and 1947, when at least one death was attributed to misguided reliance on a fraudulent cure. *Id.* at 753-754, 1060, 1298. In 1950, the FDA noted that the "search for a 'magic cure' still persists among the gullible, hypochondriacs, and sufferers of chronic ailments * * *," and that worthless preparations, including cancer remedies, have "dangerous possibilities of causing irreparable harm." FDA, *Annual Reports 1950-1974* 16 [hereinafter cited as *Annual Reports (1950-1974)*]. A public warning was issued in 1956 (*id.* at 178), and educational programs against cancer quackery were undertaken in 1958. *Id.* at 224. In 1961 and 1962 the FDA and the American Medical Association sponsored national educational programs on quackery, which was estimated at that time to cost consumers more than one billion dollars annually. *Id.* at 339-340. But in 1963 the FDA lamented that "[c]ancer quackery continues to be a major concern" (*id.* at 411), particularly among older citizens who require proper dietary and medical attention but are "often victims of charlatans and quacks." *Id.* at 439.

[34] Fraudulent cancer cures have been discussed in numerous FDA Annual Reports since 1909. See, *e.g.*, Dunbar, *supra* note 33, at 98, 118, 154-155, 312, 631, 771, 745, 841, 901, 1011, 1171, 1227, 1298, 1408-1410; and *Annual Reports (1950-1974)*, *supra* note 33, at 16-17, 72-73, 102-103, 156, 200, 247, 317, 363, 411-413, 471-472, 519, 575.

[35] Dunbar, *supra* note 33, at 101.

[36] *Id.* at 154.

burger cheese and glycerin;[37] a liniment of turpentine, oil, mustard oil, eggs and ammonia;[38] a machine housing colored floodlamps;[39] peatmoss;[40] the "Fountain of Youth," a mixture of spices, oil and suet;[41] a diagnostic kit used to analyze urine;[42] a machine delivering special electronic frequencies;[43] and mineral tablets.[44] A cancer treatment similar in theory to Laetrile was promoted in 1956 by a "nutritional expert" who claimed that cancer is a deficiency disease that can be cured by the use of certain natural vitamins which he, of course, sold.[45] The first seizure of Laetrile was made four years later, on December 28, 1960.[46]

Cancer is, of course, not the only disease for which ineffective cures are promoted. The FDA's annual reports frequently discuss fraudulent remedies for,

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[37] *Id.* at 224.

[38] *Id.* at 745.

[39] *Id.* at 1170-1171, 1229, 1298-1299.

[40] *Id.* at 1408.

[41] *Annual Reports* (*1950-1974*), *supra* note 33, at 45.

[42] *Id.* at 102.

[43] *Id.* at 317.

[44] *Id.* at 464.

[45] *Id.* at 200-201.

[46] *United States* v. *An Article of Drug . . . Laetrile (Formula L) etc.* (N.D. Tex., Feb. 7, 1961), D.D.N.J. No. 6543 (June 1962).

among other conditions, consumption (tuberculosis),[47] epilepsy,[48] diabetes,[49] arthritis,[50] and obesity.[51] The list is practically endless; it is, in large measure, the function of an available market. Polio cures evaporated with the advent of the new vaccines.[52] A similar fate befell pneumonia cures when broad spectrum antibiotics were introduced in the 1940's.[53] Until there is a general and certain cure for cancer, that disease will continue to invite the promotion of ineffective remedies.

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[47] Dunbar, *supra* note 33, at 58, 98, 152, 155, 312, 368, 606, 631, 664, 692, 711, 797-798, 820, 841, 864, 1011, 1062, 1107, 1165, 1298, 1409; *Annual Reports* (*1950-1974*), *supra* note 33, at 17, 130, 176, 200, 247, 317.

[48] Dunbar, *supra* note 33, at 155, 224, 368, 1363; *Annual Reports, supra* note 33, at 131, 176, 472.

[49] Dunbar, *supra* note 33, at 606, 693, 754, 767, 797, 864, 1004, 1060, 1062, 1107, 1166, 1225, 1298, 1359, 1410; *Annual Reports* (*1950-1974*), *supra* note 33, at 18, 73, 104, 131, 156, 176, 200, 225, 247, 277, 363, 519.

[50] Dunbar, *supra* note 33, at 1011, 1060, 1107, 1296, 1362, 1411; *Annual Reports* (*1950-1974*), *supra* note 33, at 16, 46, 75, 179, 204, 224, 247, 277, 316, 363, 413, 470, 519, 555.

[51] Dunbar, *supra* note 33, at 631, 693, 711, 1297; *Annual Reports* (*1950-1974*), *supra* note 33, at 103, 276, 414, 519.

[52] They appear to have flourished until the early 1960's. See *Annual Reports* (*1950-1974*), *supra* note 33, at 104, 200, 317.

[53] See *e.g.*, Dunbar, *supra* note 33, at 631, 664, 745, 770, 864, 893, 1108.

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